INTRODUCTION TO THE STUDY OF MEDICINE

BY

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TRANSLATOR'S PREFACE

THE rapid and marvellous developments recently made along the lines of medical sciences have rendered the task of both teacher and student increasingly difficult. It is not strange, therefore, that the medical faculty of the University of Paris has instituted a course of lectures especially intended for those entering upon the laborious study of the medical sciences.

To Professor Roger, whose experience, both with experimental pathology and clinical medicine, is of the widest range, this course was intrusted, and, as can be seen, he has accomplished the task most admirably. With this book he reveals to the student an immense horizon, presenting to him a comprehensive view of *ensemble* and constantly arresting his attention with facts and principles of paramount importance. Not alone the student, but also the practitioner who would ever keep fully abreast with the times, will find in this work a masterful *résumé* of recent medical advancement. To read it is to undertake a fascinating journey into those regions of medicine where the most important developments have recently been realized.

The chapter upon the examination of the sick will prove highly gratifying even to practitioners of considerable clinical experience.

The glossary of the French text has been omitted in this translation and an elaborate index substituted therefor.

In view of the alterations and additions which Dr. Roger kindly furnished me, this translation may be considered a second and revised edition of the work.

<div align="right">M. S. GABRIEL, M. D.</div>

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AUTHOR'S PREFACE

This book is a reproduction of the course of lectures delivered by me in 1897–'98 at the University of Paris. The object of my teaching was to lessen as much as possible the difficulties met with in the study of the medical sciences.

We all know from experience how much time is wasted by not knowing with what subject to begin, what books to read, and also by being compelled frequently to refer to a dictionary for an explanation of technical terms encountered. With the view of relieving beginners of much useless embarrassment, the Faculty of Medicine intrusted me with the course of lectures which I now publish.

The plan adopted is a very simple one. I have endeavoured to show what is the object of medicine, and by what means it may be studied. After having explained why and how an individual becomes sick, I have considered the morbific causes which constantly tend to modify the unstable state of health. These causes give rise to manifestations through the lesions and reactions they determine, some of which can be detected only after death, while others are appreciable during life. We are thus led to study the mode of reaction of the organism—namely, pathological physiology—to describe the organic changes constituting pathological anatomy, and to look for functional disturbances, the description of which forms an important chapter, semeiology.

Although I have devoted over two hundred pages to the consideration of the examination of the sick, I have done no more than present some general considerations with reference to the rules which should be followed by the physician in his practice. I earnestly hope, however, to have succeeded in demonstrating that it is pos-

sible to make a diagnosis and prognosis by simple means within the reach of all. It seemed to me important to oppose the tendency of some modern authorities who think the solution of problems raised by the examination of patients can be found in laboratory researches. No one is more firmly convinced than myself of the usefulness of experimental pathology. Nevertheless, at the bedside the physician can do no better than to depend upon clinical procedures. Only in quite rare instances will he be obliged to resort to more delicate methods of investigation. I can not admit abdication of clinical methods of investigation before the rising tide of bacteriology.

It is likewise in clinical experience that we find the indications of procedures enabling us to favourably modify the evolution of disease. This part of medicine constitutes therapeutics, to the study of which the last chapter of this book is devoted.

From these explanations it can be seen that I have, step by step, followed the course of morbid processes, thus endeavouring to construct a frame in which the descriptions of general or special pathology can be placed.

Addressing students especially, I have, as a rule, avoided theoretical discussions and reported only those results which appeared to me to be final. I have also excluded doubtful hypotheses and contestable conceptions.

Demonstrated theories and well-established facts become independent of those investigators who made them known. In proportion as science is brought to perfection it becomes impersonal; hence, I have to a great extent been able to ignore citations of proper names, confining myself to final achievements. I have explicitly mentioned only those old authorities who have made some important discovery, advanced some particular theory, or recorded some observation of consequence. Although I have on several occasions mentioned researches pursued by myself, I have, following the above rule, reported them just as I have those of other authorities, without indicating their origin. This appears to me to be the only way to avoid the unworthy questions too often raised by discussions of priority.

CONTENTS

INTRODUCTION TO THE STUDY OF MEDICINE

CHAPTER I

INTRODUCTORY REMARKS

Definition of the words medicine, health, disease—Disease and affection—The causes of diseases: division, according to the nature of the pathogenic agent, into mechanical, chemical, and animate causes; division, according to the action on the organism, into efficient, accessory, predisposing causes—Object of the various branches of pathology—The bases of therapeutics.

MEDICINE is sometimes considered as a science, sometimes as an art. Both conceptions are correct; all depends upon the view point at which we place ourselves. Medicine is a science by its means of study; it is an art by its applications. We are thus led to the following two definitions:

The object of *medical science* is the study of disease. The aim of *medical art* is to restore and maintain health.

That part of medical science which studies disease is called *pathology* (πάθος, suffering, ailment). The teaching of the medical art, as it is done at the sick bed, constitutes *clinics* (κλινικός, from κλίνη, bed).

Pathology comprises the following chapters: *Etiology* (αἰτία, cause), which investigates the morbific causes; *pathogeny*, which explains by what mechanism these causes act on the living organism to disturb its state of health or abolish its existence; *pathological physiology*, which shows how the organism reacts (morbid reactions) under the influence of pathogenic causes; *pathological anatomy*, which unveils the structural modifications resulting from the morbid actions and reactions; *symptomatology*, which gives an account of the disturbances and lesions appreciable during life; *nosology*, which describes and classifies diseases. To these different branches, which constitute the medical science, should be added two others concerning rather the medical art—namely, the technical side (τεχνὴ, art) of medicine; I refer to *diagnosis* and *prognosis*. Diagnosis (discrimination, from δια, through, and γιγνώσκειν, to know) determines the place which the disease occupies in nosology; prognosis (from πρό, before, and γιγνώσκειν, to know) tries to foretell the evolution of the disease.

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The indispensable complement of pathology is *therapeutics*, with *surgery, prophylaxis,* and *dietetics.* *Therapeutics* (θεραπεύειν, to take care) is that part of the medical art which, profiting by the scientific data furnished by materia medica and pharmacology, endeavours to relieve the sick and to modify favourably the evolution of the disease. *Surgery* is that branch of therapeutics which proposes to cure by means of manual procedure (χειρουργία, from χείρ, hand, and ἔργον, work). *Prophylaxis* (προφυλάσσειν, to watch) whose principal part is represented by *hygiene* (ὑγίεια, health), dictates the precepts to be followed for avoiding disease. Dietetics (δίαιτα, *régime*) indicates the diet conducive to the restoration or preservation of health.

Pathology embraces, then, nearly all of medicine. There is a manifest disproportion between its vastness and the limitations of the human mind; hence the necessity of dividing its study into several distinct branches. The following divisions are generally admitted: *Special* or *descriptive pathology,* which makes an analytical study of diseases and comprises *internal* or *medical pathology* and *external* or *surgical pathology; comparative pathology,* which takes into consideration diseases in man, in animals, and even in vegetables; *experimental pathology,* which proposes to modify the evolution of spontaneous diseases and to reproduce, with a view of explaining and combating them better, the disturbances, lesions, and diseases with which we have been acquainted through observation; finally, *general pathology,* which defines the terms and fixes their meaning, determines the laws of morbid phenomena, investigates the causes, processes, and symptoms, and classifies them. It outlines the rules of nosology, and prepares the frames in which special pathology will place its descriptions. Although general pathology is often considered as the synthesis, that is, the loftiest part of medical science, and often rises to sublime conceptions well calculated to seduce and captivate the mind, it may well be contented with more modest views; it may be elementary and furnish the beginners with rules to guide in their studies of diseases. When we know which are the morbific causes most frequently intervening, when we are sure of their mode of action and have understood the mechanism of morbid reactions, derangements, symptoms, and lesions, we are prepared to understand and appreciate particular cases.

We have repeatedly made use of the words health and disease. These two words are currently employed; but, while there is a universal agreement as to their meaning, there arises considerable difficulty when an inquiry is made into the precise nature of phenomena designated by these terms. The same is true of all abstract ideas: only those subjects are well defined whose limits can be comprehended by the mind. Health and disease (or *hygid state* and *morbid state*) are connected

by a multitude of disturbances more or less well characterized; it is therefore very difficult, not to say impossible, to draw a sharp line between these two states, which, absolutely different in their highest expressions, approach and unite with each other in their attenuated manifestations. The difficulty is rendered greater by the fact that perfect health does not exist; living organisms are always in a state of unstable equilibrium, which finds its explanation and cause in the very conditions of life.

It is known, in fact, that living matter is the seat of a series of acts which do not depend, as was once believed, upon a vital force animating matter, but should be considered as reactions produced by the variations of external agents.

Let us suppose for a moment that no modification whatever is produced in the cosmic forces, no change at all in the relations of a being with the objects that environ it: equilibrium will soon be established between this being and the surrounding world. Of course, life is not annihilated under these conditions; but it remains latent, as was once said, or, to speak more correctly, remains in a static state. But the moment an external variation occurs, the equilibrium is broken; the living organism, to adapt itself to the new conditions, presents a series of reactions making life again apparent—that is, causing it to pass into the dynamic state. Now, in reality, the cosmic forces constantly vary, the objects are displaced and modified; the world we live in changes, and, life being but an adaptation to medium, living matter is incessantly agitated by reactionary oscillations calculated to counterbalance the influence of the external agencies. Thus is explained the unstable state just referred to.

If neighbouring variations are slight and slow, adjustment is readily made and health preserved. Should they be intense and sudden, compensation becomes more difficult, often resulting in indisposition, sickness, or death. Let us suppose, for example, a man placed in a room with a fixed temperature of 20° C.; the organism of this man is regulated so that the production and dissipation of heat maintain his organic temperature at 37° C. As the medium is supposed to be constant, heat production will be managed also in an invariable way. Suppose, now, that the temperature of the room rises or falls one degree; the equilibrium is disturbed and thermogenesis modified. In order that his temperature may always remain at 37° C., he must either produce more heat or expend less. When the variation is light and progressive, adjustment is made easily and unconsciously; the organic modifications are not perceived and do not cause any trouble. But if the temperature of the room should suddenly rise from 20° to 80° C., or fall to — 40° C., this change of 60° in plus or minus would

completely upset the thermogenic equilibrium of the organism and provoke a series of disorders resulting in disease or a fatal termination.

What we say about heat can be repeated with regard to other physical agents. Barometric variations, imperceptible when slight, give rise to indisposition when intense. If it is a question of considerable change of pressure—for instance, when making a balloon ascent, or when one is submitted to the action of compressed air, and especially when one is caught in a gas explosion—the accidents may prove very serious, or even fatal.

Physical variations are not the only ones capable of impressing the organism; all modifications occurring in our relations with surrounding objects and beings may produce the same effect. It is therefore possible to transport into medicine the classical data of the physical and natural sciences and divide the pathogenic agents simply into four groups: Mechanical agents; physical agents; chemical agents, including the caustics and the toxics; animate agents, subdivided into parasitic and infectious (the latter including most of the pathogenic bacteria). This enumeration shows that diseases are not provoked by new, special, mysterious causes, but by the ordinary cosmic agents—by the objects and beings that surround us. When impressed by these various agents, the organism, as above noted, does not remain indifferent; it responds by reactions, whose purpose, if not the effect, is to bring the economy to a state compatible with life. Therefore two orders of phenomena are to be noticed in every disease: those due directly to the cause and those referable to the reaction of the organism. The latter are far more important than the former. In a good definition, however, we must, following Dr. Bouchard, take into account both series of morbid manifestations. We are thus led to the following definition:

" Disease is the *ensemble* of the phenomena which are produced in an organism undergoing the action of a morbific cause and reacting against it."

We have thus far supposed this morbific cause to be *exogenous*—i. e., outside of the organism. But authors often attribute disease to internal or endogenous causes—that is, causes taking origin within the organism. We have excluded this etiological group for the reason that it is no longer acceptable; all diseases, indeed, proceed from an external cause. The opposite view is due to a persistent confusion of disease with affection.

Take, for instance, a man suffering from typhoid fever. The disease being over, the organism is restored to health. But the restoration is only apparently perfect; modifications persist which, too slight to be perceived, follow nevertheless their progressive evolution. Ten, fifteen,

twenty years later, new manifestations break out—for example, some disturbances due to heart lesion. By that time the disease is almost forgotten, and, as no intermediate bond connects the actual manifestations with the disease left far behind, considerable difficulty is experienced in tracing the succession—some sort of repugnance to connect this cardiopathy with the long expired typhoid fever. In another case the subject will have been through a number of different diseases, and the physician will be at a loss as to which of them to attribute the new visceral disorder.

From a philosophical point of view it is essential to reascend to the first disease. From a practical standpoint this inquiry is often useless. Whatever the etiological conditions may have been, the effect is the same. Organic affections are simply cicatrices; disengaged from the initial cause, they become autonomous and develop on their own account.

Let us take up the example above referred to. Suppose a man suffering with a cardiac affection. Whatever the starting point of the cardiopathy may have been, whether rheumatism, typhoid fever, or any other disease, the effects are identical. The new morbid manifestations derive no particular character from their origin. The etiological notion is of no practical importance, but is indispensable to the nosologist who will even refuse to consider the affections of the organs as diseases.

What is true of the heart is true of all the viscera. Their affections take origin from some antecedent cause. For a long time this very simple truth has not been understood because the initial disease is not always easily found out; the visceral derangement may be the first outward manifestation, leading to the belief that it is making its appearance spontaneously.

To those who should wonder how a visceral lesion is capable of developing silently for twenty or thirty years without giving rise to any symptom, we can answer by the well-known example of gonorrhœa. A man has a urethral discharge at the age of twenty; he recovers in a few months, and seems to be completely cured. Toward the age of forty or fifty micturition grows difficult, and a urethral stricture is discovered, which nobody hesitates to connect with the former attack of gonorrhœa. It is a remnant of the infectious process, a cicatrix that has shrunken little by little. Why, then, should we regard as doubtful in the case of the viscera and organs that which is so readily admitted to be true as regards the urethra? The process is alike in both cases; it is one of cicatricial evolution, slow and progressive.

We can therefore, in the presence of these tardy manifestations, sequelæ of diseases, isolate the exciting cause; but on condition of being

mindful of the fact that the actual disorders are due to an anterior cause which voluntarily we disregard.

When the actual morbid process is considered without taking into account its initial cause, the name disease can not be applied to it. It is preferable to employ the term *affection*. We shall define, therefore: " *Disease* is the morbid process considered in its entire evolution, from its initial cause to its final consequences; *affection* is a morbid process considered in its actual manifestations, apart from its cause."

It is improper to speak of diseases of organs; affection is the proper term. Some authors use, in this sense, the term *pathy* as a suffix following the name of the organ. The word thus created indicates an affection of this organ, without prejudging the disease. This procedure, strongly advocated by Dr. Landouzy, is perfectly rational. The words *cardiopathy, pneumopathy*, etc., have the advantage of being both well constructed and very suggestive; " cardiopathy " is simpler than " cardiac affection " and more exact than " heart disease." This nomenclature would put an end to the confusion that has been established and maintained between disease and affection.

Another condition further complicating the problem is the fact that the modifications produced by diseases and affections may influence the descendants. Thus is created morbid heredity, which may be transmitted through a great number of generations, and may explain the development of pathological families. Variously tainted children are brought into the world, presenting a defective nutrition and predisposition to certain diseases. In this event the disturbances of health are autogenous so far as the sufferers themselves are considered, but in reality they are exogenous in that they are the result of external influences exerted upon their parents. In pathology, as in biology, the successive series of livings beings must be considered as a single being eternally existent.

We shall consider at length, in a later chapter, the rôle of heredity, which explains a group of causes which, at first sight, seem to form an exception and to depend upon an internal origin. I refer to psychical causes. Psychical phenomena, the highest manifestations of life, appear to be independent of the external medium. In reality, though more complex, they do not differ essentially from bodily phenomena; they are equally dependent upon external agents which have acted upon the person himself or his ancestors.

These considerations amply authorize us to reject absolutely the division of morbific causes into internal and external. The initial causes are always to be looked for outside the organism. In view of their nature they may, as we have said, be classified into four groups:

Mechanical, physical, chemical, and animate causes. In view of their action upon the organism, it is possible to divide them into *effitient* and *predisposing causes.*

The *efficient causes* are always necessary; at times they are sufficient by themselves. Let us take, for example, the anthrax bacillus, which is one of the microbes best studied by experimenters. Let us introduce it beneath the skin of a guinea pig. The animal contracts the disease and dies within three or four days. In this case the efficient cause has proved sufficient. Let us make the same inoculation into a more resistant animal, the white rat. No disorder will be produced. But let us submit this white rat to some fatiguing exertion, or inject into it some toxic substance. The intervention of such an accessory cause will favour the action of the efficient cause: the anthrax will develop. The more we study pathology and get an insight into the history of infections, the better we understand the importance of auxiliary causes. There are certain microbes which develop as soon as they are deposited on a wound or even a healthy mucous membrane, but they are exceptions. In most instances various causes must come to their assistance. This is especially true of the microbes inhabiting our normal bodies. Our integuments and mucous membranes swarm with innumerable pathogenic agents, which vegetate as simple innocent parasites until the day when an auxiliary or, as some still say, a determining cause permits them to overcome our resistance and exercise their noxious influence; then appear a series of acts ending in indisposition and disease. Pneumonia, for example, is an infection induced by a microbe frequently present in the mouth of healthy persons; so long, however, as the organism is in a normal state the microbe can not develop. But let some common cause—fatigue, cold, or inhalation of irritating vapours—reduce the resisting power; the microbe, until then harmless, becomes pathogenic. This well-known example proves that the co-operation of the two orders of causes is indispensable. Let us not fall into the error of the first bacteriologists, who thought the microbe was sufficient to explain all; an error less excusable than that of the ancient authorities, who, having no idea of the rôle of animate agents, explained morbid phenomena by the intervention of auxiliary causes alone; and hence they believed also in morbid spontaneity. They believed in it also because they did not understand the nature and mechanism of predisposing causes. They assigned to predisposition an internal origin instead of seeing in it the resultant of impressions made upon the subject or his progenitors by external causes having acted antecedently. Predisposing causes are antecedent causes with respect to present disorders; efficient and auxiliary causes are present causes.

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Each pathogenic agent may play alternately the part of efficient cause and of auxiliary cause; heat and cold, for instance, in mortifying a tissue, act as efficient causes, but they fall into the order of auxiliary causes when they favour the development of a microbe. Likewise a microbe or a poison may produce a disease or aid another pathogenic agent. We should never lose sight of the possibility of these etiological associations, these morbid synergies which play a part extremely important in pathology.

According to the mode and extent of their action, the pathogenic causes are often divided into *local causes* and *general causes*. The former act on a limited point of the organism, the others act on the entire economy, or rather on numerous points thereof. The same pathogenic agent may enter into either of these groups. For example, streptococcus, a kind of microbe, when inoculated subcutaneously, produces a local lesion—erysipelas; when injected into the veins, it gives rise to a general infection—i. e., septicæmia.

Every local lesion presents to study two orders of phenomena: those occurring at the point of application of the cause and those produced in distant parts.

At the point where the agent acts, the cellular elements are irritated, altered, or destroyed. These first disturbances, provoked directly by the pathogenic agents, give rise secondarily to responsive phenomena in the elements that remain alive. These manifestations constitute what Dr. Bouchard calls *primitive autonomous elementary dystrophies*.

But the organism is so constituted that a lesion can by no means remain local; it soon arouses a series of secondary manifestations, of which some are due to nervous reactions, others are caused by the absorption and penetration of anomalous substances produced at the primary focus. These secondary morbid manifestations represent pathogenic processes of a second order. They result in the formation of new lesions and the production of new disturbances, which become themselves the starting point of manifestations of a third order, and so on. The pathological process is thus liable to become extremely complicated. These successive manifestations are of course of an internal order; only the starting point (the *primum movens*) of the morbid series has been an external cause.

The study of morbid reactions, of which we have outlined the mechanism, constitutes *physiological pathology*. It is not to be supposed, however, that these reactions are essentially different from those observed in a physiological state. Biological laws are the same in both morbid and normal phenomena. It would be an error to believe that the living being is able to dispose of different manifestations, some of

them intended for normal conditions, others for pathological conditions. The mode of reaction is ever the same; the results vary only in their intensity, but they are directed toward the same end—i. e., they always tend to counterbalance the action of external forces. In other words, health is organic reaction in fixed and pre-established conditions; disease is represented by reactions of the same nature, but produced in variable and new conditions. While the causes vary, the reactions may remain the same in their essence, notwithstanding the dissimilarity of their manifestations. Pathological physiology must not, therefore, be opposed to, but simply considered as the consequence of, normal physiology.

The morbid actions and reactions express themselves by functional modifications and structural lesions, which may be recognised during life or discovered only after death. The *structural lesions*, the study of which constitutes *pathological anatomy*, must be considered as the result of functional disturbances; as we are taught in general biology that it is the function that creates the organ, so in pathology it is proved that the disturbance of the function is responsible for the organic lesion.

Disturbances and lesions may, as above stated, be disclosed during life; they then constitute the *symptoms* and *signs* of the disease, and, according as they are perceived by the patient or recognised only by the observer, are divided into subjective phenomena and objective phenomena. In order to study them, we usually begin by interrogating the patient and making a list of his subjective symptoms; next we proceed to observe the objective signs by passing systematically in review all the apparatus and all the organs. Then comes the task of resolving the final problem: the symptoms presented by the patient being given, to recognise the disease. A difficult problem, indeed, because error may be owing to a bad determination of symptoms as well as to faulty interpretation of their relative value. Doubtless there are certain cases in which the recognition of a single phenomenon suffices to settle the diagnosis; the symptom is then called *pathognomonic*. But this is exceptional. The relative significance of the different symptoms must be determined, or, as is sometimes said, their *semiological value* established. When we are through with the methodical analysis of the patient, we must make the synthesis of the disease, connecting each trouble with its immediate cause, determining the nature and mechanism of the latter, and thus ascending the entire scale of successive manifestations until we reach the affection or disease which has been the point of departure of the morbid series.

Let us take an example: A man is complaining of pain in the side. This subjective phenomenon leads to an examination of the respiratory

organs. On auscultation, râles are heard at the base of the lung, indi-
cating congestion. But pulmonary congestion is not a disease; the
cause of the trouble is to be looked for. So, pursuing the examination,
we find out that this man has a cardiac lesion and that the pulmonary
manifestations are due to the insufficiency of the heart. If we had
seen no more than the congestion of the lung we might, by treating
this organ, have done some good to the patient, but we would not have
cured him. Having recognised that all depends upon the heart, we may
act upon the cause of the disturbances and obtain far better results.
By making the diagnosis of cardiopathy, the clinician has thus far
done enough for practice, but the nosologist has not completed his
task. He knows there is no organic disease; he must, therefore, discover
the cause of the cardiac lesion. Questioning the patient brings to light
the fact that he has once suffered from an infectious disease, typhoid
fever or acute articular rheumatism, which has given rise to endo-
carditis; this explains all. We have discovered the primary disease, of
which the present affection is but the sequel. So far, however, as
treatment is concerned, this disease is of no importance; the patient
is not suffering from typhoid fever or rheumatism, but from a cardi-
opathy, and the medication will be the same, no matter what may have
been the cause of the affection.

It is not to be supposed, however, that it is useless to inquire into
the causes. Here is a man who has lost the faculty of speech; he is
attacked with aphasia. Now, aphasia is dependent upon a lesion of the
third frontal circonvolution of the left side. Taking our stand upon
antecedent or concomitant troubles, we diagnosticate a tumour pressing
upon the cortical centre of speech. If we stop there in our diagnosis,
we shall have recognised a cerebral affection, and might tell the patient
there is no efficacious treatment for it. But, pushing farther our
analysis, we discover on the skin old cicatrices revealing the existence
of an ancient syphilis. At this point our diagnosis is complete, and
leads us to institute the specific treatment which will cure the patient.
In this case inquiry into the causative disease has led to the etiological
therapeutics which alone could be successful. The determination of an
exact and complete diagnosis is attended by that satisfaction which is
always experienced when a difficult problem is solved; but, what is of
greater consequence, it furnishes the precise indications of treatment.
Unfortunately, in practice, the physician is not appreciated according
to his skill in determining the nature of a sickness. What the patient
and his friends require of him is prognosis; they are, of course, unable
to verify his diagnosis, but they witness the course and termination of
the sickness, and according as his predictions are realized or not they
conclude that the doctor was right or mistaken.

In a great number of instances prognosis and diagnosis are connected. A child, for example, presents certain symptoms which lead us to diagnosticate tubercular meningitis; the prognosis is then well-nigh fatal. On a more careful examination, some rather odd phenomena might be discovered, and, auscultating more attentively, there might be heard a tubal murmur in the thorax. It was not, therefore, a question of meningitis, but simply meningeal accidents dependent upon pneumonia. The termination will be altogether different—the patient will recover. In this case the error of prognosis is connected with the error in diagnosis.

Prognosis is not always deducible from diagnosis. Besides diseases with a well-nigh fixed prognosis, there are others in which prognosis totally varies with the forms, the epidemics, the concomitant phenomena, and the previous state of the subject. On all these questions there can be given some general notions that may materially help, but for the matter of prognosis, as well as of diagnosis, books and lectures are inadequate. The medical art may be learned only by practice. It is only by seeing many patients and comparing different cases that one acquires the habit of weighing the value of signs which lead to correct diagnosis and prognosis.

In establishing the prognosis, the expected influence of the treatment should also be taken into account. The therapeutic indications are derived from the study of symptoms, causation, pathogenic process, and pathological physiology. We may, then, according to the indications which serve as our basis of treatment, admit a symptomatic, an etiological, a pathogenical, and a physiological therapeutics.

Symptomatic therapeutics aims to relieve painful symptoms, functional disorders, and to combat immediate accidents; it appeases and assuages, but seldom cures.

Etiological therapeutics fights the very cause of the evil; it furnishes antidotes, vermifuges, antiseptics. The method of treatment is etiological when specific remedies, such as mercury for syphilis, quinine for intermittent fever, and salicylate of sodium for rheumatism are prescribed.

The morbific cause is often beyond our reach, either because we are unable to touch it by our present procedures or because its action has been transitory; we must therefore act on the mechanism set in action by the cause or on the reactions presented by the organism. This would be *pathogenical* or *physiological medication*. This is what is realized when an attempt is made to restore to the normal rate nutrition disturbed by various causes, or to modify nervous reactions, or to neutralize the effects of microbic toxines.

The therapeutic ideal is to realize these rational medications. But at present, while it is easy to lay down general indications, it is oftentimes impossible to fulfil them; the physician must content himself with symptomatic treatment, at times even with empiricism. He must still resort to statistics, whose data are indispensable in reassuring him as to the value of treatments; he thus secures some tentative results, which he will abandon as soon as the advance of science enables him to substitute rational for empirical medication.

We conclude, therefore, that the interest of the study of general pathology is not merely a speculative one. It alone can supply guiding ideas which will serve as the basis of the medical art.

CHAPTER II

MECHANICAL AGENTS

Medical definition of mechanical agents—Mechanical agents acting by pressure: punctures, cuts, contused wounds—Commotion—Compression—Mechanical agents acting by distention—General reactions—The influence of passive movements—Seasickness.

FROM a medical standpoint, mechanical agents may be defined as " all those that tend to modify the state of rest or motion of a portion or the entirety of a living body—i. e., to modify its position in space."

There may be three examples:

1. The mechanical agent is a body in motion; it encounters a living being opposing a resistance to it.

2. The mechanical agent represents the resistance, and the human body the power. Such is the case when a man falls from a certain height.

In these two instances, although the mechanism is different, the result is the same. There is a conflict between power and resistance.

3. The third group, of far less importance, comprises those agents tending to impart motion to the whole body, as occurs when we find ourselves on a moving object or a boat agitated by the sea.

Let us consider first the results of the conflict ensuing between an agent in motion and a living being. It is said in mechanics that such an agent is endowed with kinetic energy. This force is equal to half the product of its mass into the square of its velocity, as expressed by the well-known formula—$E = \dfrac{M V^2}{2}$.

This formula has considerable interest for us.

Let us suppose a missile having a mass equal to a unit whose speed at the moment it reaches the living body is equal to 1; the energy will evidently be represented by $\frac{1}{2}$.

If the mass becomes 20, 100, 1,000 times greater, the velocity remaining the same, the energy increases as half of these figures and becomes 10, 50, 500 times greater.

If the velocity increases in the proportion of 20, 100, 1,000, the energy increases as half of the square of these figures—i. e., as 200, 5,000, 500,000. Thus, while the mass increases as 1,000, the energy increases as 500; the velocity increasing as 1,000, the energy increases as 500,000. This clearly shows that the effects produced by the wounding body are directly in relation to the velocity acquired. Here is the whole secret of the action of mechanical agents, and notably of fire-arms. A bullet of the Lebel rifle is 8 millimetres in diameter and weighs 15 grammes; the ravages which it produces depend merely upon its velocity, which, at the starting point, is 631 metres per second and is expressed by an energy of 344 kilogrammetres.

In order to understand the action of mechanical agents, we must take into account two factors: their power—i. e., their energy—and their direction.

The power of a wounding agent is easily determined. Besides its speed, we have to consider its mass or, what is simpler, its weight, its density, and its volume. We must, moreover, take into account its form, and the projections or inequalities of its surface. We can not dwell upon the importance of the various conditions just enumerated; it is not difficult to understand their multiple effects. In the case of a war projectile it is quite certain that, assuming the energy to be the same, the injury produced will be the less serious the less voluminous, the smoother, and more resisting the wounding body is, so as to pass through the tissues without bursting.

The effects vary also according to the direction of the mechanical agent—i. e., according to the angle at which it strikes the living being. A projectile may enter a member of the body perpendicularly, obliquely, or parallel to its axis. The oblique course is evidently longer and causes far greater injury. In the case of a parallel course, the projectile may simply run beneath the skin without touching any important part.

In order to introduce harmony into the study of mechanical agents, it has been necessary to adopt a certain number of divisions. Two great classes may be admitted, according as the pathogenic agent acts by pressure or by traction.

Mechanical Agents acting by Pressure

The mechanical agents acting by pressure are the most important. They are divided into three groups, according to the extent of their surface of contact. According as they terminate in a point, a line, or a plane, they are designated as puncturing, incising, or contusing agents.

Punctures.—A puncture may be produced by very slender objects, as needles, pins, cannulæ of hypodermic syringes, by splinters, or the

sting of certain animals, insects, arachnida, and scorpions. In other cases they are due to instruments with an abrupt enlargement above their termination—e. g., swords. The effects differ, of course, according as the puncture is a small or a large one.

In the first instance no notable accident is generally produced. The puncture with a needle, or a pin, or a splinter causes slight pain, loss of a drop or two of blood, and then cicatrization is rapidly effected. No greater harm results when the objects are a little more voluminous, as bodkins or various instruments employed in the industries. The only danger is that the pricking agent may be charged with toxic substances (poisonous punctures, poisoned arrows) or contaminated with microbes, which invade the little wound. Such punctures, designated as *septic*, will be considered in connection with infections.

It may also happen that the instrument remains in the wound, as is particularly the case when it breaks. The foreign body may remain for years in the tissues without giving rise to any inconvenience. Sometimes the agent wanders in the organism and finally protrudes in a region often very far removed from the point through which it originally entered.

In a general way, it may be stated that the tissues tolerate foreign bodies that have merely a mechanical action. The exceptions to this rule are only apparent. Several experimenters have seen nodular lesions, analogous to tubercles, develop around grains of lycopodium, Cayenne pepper, and oyster shells. It must be admitted that in such instances the foreign body had not acted in a merely mechanical manner; an infinitesimal part underwent solution and excited irritation in the neighbourhood. Although it may be objected that the question is often one of insoluble bodies, it must be remembered that numerous researches have established the fact that living cells are influenced by quantities of substances so minute that no chemical test can detect them. Bodies reputed to be insoluble may in reality be dissolved in a quantity sufficient to give rise to reactions on the part of the organism.

It is well to recall here the brilliant experiments of Raulin, who proved that the aspergillus can not grow in a silver vessel. The liquid contained in the vessel dissolves an amount of the metal which no reagent except the living cell can reveal. Naegeli likewise established the fact that a gold coin placed in a glass of water diffuses sufficient copper to arrest the development of spirogyra. One part of a copper salt per 1,000,000,000 suffices to cause the plant to perish. These results are not only of interest to the naturalist; they lead to the admission that foreign bodies, whatever they may be, exert no pathogenic action except when they pass into solution. A foreign body which remains

absolutely insoluble will be tolerated by the tissues and call forth no reaction.

To return to the mechanical action of pricking bodies. We have to consider the effects produced by them on various parts of the organism. Let us first direct attention to the blood vessels. Punctures are well borne by these structures. Blood is quite frequently drawn from veins for diagnostic purposes. A Pravaz syringe cannula, for instance, is introduced and a small amount of blood withdrawn. This method, which had already been employed by Davaine, is often employed at present, and never causes any accident when the needle is aseptic. Likewise, intravenous injections may be practised on man, as well as on animals, by the introduction of a cannula through the unbroken integuments. A little ecchymosis, if anything, is produced, which, however, is of no importance.

Puncture of arteries is just as harmless. The muscular coats of these vessels insure perfect closure. Intra-arterial injections may be made in this manner in animals, at least in dogs. In rabbits, however, the musculature is insufficient, and puncture of an artery by means of a Pravaz needle gives rise to very grave hemorrhages.

In man, puncture of aneurismal sacs is frequently practised. Very fine needles, called Japanese needles, electrodes, and watch springs are introduced. The wound is too small to allow the escape of blood.

Even the heart has been punctured. The experiments of Sanctorius, of Plater, and especially those of Bretonneau and Velpeau, established the possibility of the introduction of needles into the heart of animals without danger. At the present day experimenters in physiological laboratories frequently make use of long needles terminating in a little flag. These are thrust into the cardiac cavities in order to observe the movements of this organ. Practised on dogs and rabbits, this experiment is unattended by bad effects, and it does not even seem to be painful. In view of these experimental results, it has been proposed to practise abstraction of blood from the heart in man. This therapeutic measure, consisting in the introduction into the right ventricle of a thin needle connected with an aspirating apparatus, can not be accepted without reservation. For even if it be true that in most cases puncture of the heart is harmless, that pins and sword points have been found in this organ which endured them without inconvenience, still such is not always the case. Some persons have suddenly succumbed in consequence of a simple, nonpenetrating wound (as in the famous case of Latour d'Auvergne). An observation of Dr. Magnan is very interesting in this connection: An insane woman succeeded in committing suicide by means of a pin, three centimetres long, which she drove into her heart at the level of the apex. At the autopsy it was

seen that she had made eight punctures in her heart, but none of them had traversed the muscle.

Puncture of a nerve causes intense pain, and, what is of more importance, it may be followed in certain instances by a rebellious neuralgia.

Puncture of the nervous centres is not serious except when it touches the point described by Flourens under the name *nœud vital*. Then it causes sudden death through arrest of respiration. In several instances criminals have killed their victims by puncturing them at this point. In this manner, also, a certain number of infanticides have been perpetrated.

Punctures of the viscera do not generally produce any accident. For purposes of clinical exploration or therapeutic intervention, the spleen, liver, and lungs have often been punctured. In emptying a hydrocele the trocar has perchance been driven into the testicle without any harm resulting.

Even when a reservoir full of liquid is punctured, closure is easily effected. In cases of retention of urine, the bladder is frequently punctured, and even the intestine has been submitted to the same operation. In the latter case the puncture is closed by a little hernia of the intestinal mucous membrane; not a single drop of the intestinal contents escapes into the peritoneum. This fact has been applied with benefit in the treatment of tympanites caused by intestinal obstruction. But the procedure is not altogether free from danger, and it has therefore been abandoned. Lastly, from a medico-legal standpoint, it is well to remember that puncture of the fœtal membranes by means of a needle introduced through the cervix of a gravid uterus is one of the procedures most frequently adopted to induce criminal abortion.

In the case of large punctures, such as those produced by a sword thrust, the effects are often without gravity, especially when the wound is situated in a limb.

Wounds of the two great cavities of the body are divided into *non-penetrating* and *penetrating*, according as the wounding agent stops in the wall or traverses it. In the latter case the wounds are designated as *simple* or *complicated*, according as the viscera are involved or not. In some instances swords have passed through the thorax or the abdomen without touching the organs. Such occurred in the case of a young man presented by Després at the clinics of Bérard (1843). He fell from a cherry tree, 3 metres high, upon a prop which penetrated the back and made its exit above the pubes, fixing itself farther in the thigh. Passers-by removed him from the pole and he was taken to a hospital, where he rapidly recovered.

A sword may pass through the thorax, making its way across the

pleura without separating its layers or giving rise to a pneumothorax. In certain cases the sword may strike the vertebral column and there be broken. It may then become encysted at this point without inconvenience, even though it has passed through the lung. Velpeau had the opportunity of making an autopsy upon the body of a man who had had a foil broken in his thorax fifteen years before. He found in the interior of the lung the iron blade, which measured 8.5 centimetres in length.

However, when the organs are injured certain disturbances are generally produced, among which two phenomena are most important—namely, hemorrhage, sometimes sufficiently profuse to cause death, and, in case of injury to intra-abdominal reservoirs, escape of the liquid contents from within the wounded organ.

Cuts.—Cuts are solutions of continuity produced by instruments, such as knives, saws, sabres, and also by splinters of glass and pottery. In this group are to be included the cuts sometimes caused by a sheet of paper or a tensely stretched wire. Finally, although the mechanism is more complex and the cut may be complicated with contusions, we may add to this list the great damage caused by the horns of animals, notably of cattle.

In order to recognise the nature and gravity of the accidents produced by cutting agents, we must take into account their weight, the force with which they strike, and also their direction. If a knife is simply thrust into the tissues the wound produced is much less grave than when care is taken to modify its direction after introduction—i. e., to raise or lower the handle. Under such circumstances the person using the knife is more certain to strike some important organ and to injure it to a great extent.

All tissues are not affected in the same manner by cutting instruments. In this regard the following rules have been established: Tensely stretched parts are incised; soft parts are crushed; hard parts break. These formulæ, however, are not absolute. In certain instances a bone, instead of breaking, is penetrated by the cutting instrument, and the latter may even break off and remain in the osseous tissue.

Unlike punctures, cuts often involve the blood vessels and may give rise to hemorrhages. The hemorrhages are the more profuse the cleaner the incision is, the more firmly the vessel is fixed to the neighbouring parts, and, consequently, the less tendency it manifests to contract. In certain regions—e. g., in the neck—the veins being held open by the cervical aponeurosis, air may enter and produce accidents, which will be referred to in connection with gas emboli.

When the cutting instrument incises a nerve we observe, in addition to the immediate pain, an anæsthesia or a paralysis affecting the region

to which the nerve is distributed. These accidents are not incurable; for, on the one hand, the severed ends of the nerve may again be united, and, on the other, a functional supply is re-established through the agency of the numerous anastomoses connecting the various portions of the nervous system.

When any one of the great cavities is incised, the wound, as in the case of punctures, may be nonpenetrating or penetrating, and in the latter instance it may be simple or complicated. Even though the wound does not involve any organ, it is much graver than a puncture, because it exposes the individual to a new accident, to hernia—i. e., the escape of the viscera. If the thorax is wounded, the lungs may protrude; if the abdomen is incised, the intestines and the omentum; at times the stomach, spleen, and bladder may escape. It is hardly necessary to say that such complications are of a grave nature, since they lead to contamination and infection of the protruded parts.

When a limb is incised, the solution of continuity leads to modifications, which must be well recognised, and which are explained by the contractility of the tissues. Suppose a limb is cut off in a plane perpendicular to its long axis; the resulting stump assumes the aspect of a cone the apex of which is represented by the bone and the base by the skin. This result is to be explained as follows: The bone is, of course, not displaced; the deeper muscles adhering to the bone and retained in position by the aponeuroses have retracted very little; the superficial muscles, being more loosely attached, have retracted, and the skin, being far more contractile than the other tissues, has shrunken to a degree greater than all the subjacent parts. Therefore, in order to avoid a conical stump, it is necessary to incise the skin at a point farther down the limb than where the superficial muscles are severed, the latter farther down than the more deeply situated muscles, and the deeply laid muscles just beyond the cut end of the bone.

In retracting, the muscles cause the cut ends of the tendons to recede into their sheaths, so that it is often difficult to bring their severed portions into contact.

The contractility of tissues does not always act unfavourably. The contractility of the coats of the vessels plays an important part in hemostasis. When an artery is severed the external coat does not change its position; the middle coat, however, retracts, and in this manner diminishes the calibre of the vessel, thus favouring the formation of an occluding clot.

In other instances the contractility of the tissues hinders reparation. This is what happens when the trachea is incised. On transverse or even incomplete section of this structure the two lips of the wound retract, and this naturally prevents cicatrization. With the intestines

the effects are similar but far graver, for the gaping of the wound permits the escape of fæcal matter into the peritoneal cavity.

When incisions are quite clean they very readily heal as soon as the separated parts are united and retained in position by sutures. It is then said that the wound heals by *first intention*. Such wounds, however, may become infected and open a route for bacteria. Such an occurrence is comparatively rare, for the clean-cut tissues preserve a very high degree of vitality and oppose the development of pathogenic agents, as when under normal conditions. Between what obtains here and in the case of contused wounds there is a very decided difference.

Contused Wounds.—*Wounds caused by Firearms.*—As already stated, the contusing agents are those which come in contact with our bodies by a blunt surface.

Of contused wounds, the most interesting are those produced by firearms. Let us, therefore, begin with their study. After having indicated some general principles applicable to all firearms, we shall consider the effects caused by the new projectiles.

In every wound caused by a bullet three parts are to be taken into consideration—namely, the point of entrance, the tract, and the point of exit. When the ball has lodged in the body there is evidently but one orifice, and the tract is therefore said to be blind. The wound at the point of entrance is always smaller than at the point of exit; it is even smaller than the diameter of the projectile. This phenomenon is due to the elasticity of the tissues. On the other hand, the aperture of exit is larger than the diameter of the ball; its diameter may be two to three times greater, and may attain to from 10 to 15 centimetres. The wound at the point of entrance is regular, with clean edges; the wound of exit is lacerated and often gives out particles of muscle and fragments and granules of bone. The tract of the bullet is direct or tortuous. It is direct when the missile is driven with great force through all the parts it encounters; it is tortuous when the speed of the bullet has been reduced and it ricochets over a bone.

After having fractured a bone, a ball may impart to the fragments sufficient force to cause them to act as glancing missiles and aggravate the lesion by enlarging the wound. Fragments and granules of bone and particles of muscle are real foreign bodies, which must be eliminated in order to make cicatrization possible. The wound may also be contaminated by solid substances, such as pieces of clothing, stones, and sand, which have been introduced from without. Moreover, the projectile may lodge in the tissues; it not infrequently breaks up, and each fragment then produces further disorganization in diverse directions; or a fragment may escape outward, thus leaving an aperture of exit

and giving rise to the erroneous assumption that the projectile is no longer to be looked for in the wound.

Bullets may produce three types of fractures in bones. In some instances the bone is simply perforated. If the cranium is the seat of injury there may be found two clean orifices, one corresponding to the point of entrance, the other to the point of exit of the projectile, the latter by far the larger. At other times the bone breaks by contact; the fracture may be clean, as if cut with a sharp instrument; oftener it is comminuted—i. e., the fracture at times consists of a considerable number of fragments, or, as is frequently stated, of splinters. In higher degrees there is a true bursting of bone. Lastly, the third variety is produced when the bullet strikes the bone in a direction almost parallel to its long axis and cuts a veritable groove in the diaphysis.

It is readily understood that a projectile moving at a low rate of speed, instead of breaking a bone, may lodge in it and flatten out; in other instances it may be diverted from its course, as is often the case when a revolver is discharged at close range at the thorax or the skull. Under such circumstances the bullet may follow a rib or a bone of the cranium without penetrating the cavity. In such instances it produces a subcutaneous " seton wound," which readily heals.

Wounds of the arteries give rise to very grave hemorrhages. The statistics of the Crimean War show that in 18 out of 100 cases death was due to this cause.

Finally, when a ball strikes an organ it may produce three varieties of lesions: a perforation, a laceration, or a crushing of tissue, which is then truly pulpified.

Several hypotheses have been advanced to explain the action of projectiles.

Melsens attributes an important rôle to the stratum of air which forms a kind of sheath around the ball, at least when its velocity exceeds 340 metres.

Kocher compares the resistance of tissues, particularly of bones with cavities containing marrow and blood, to that of a wooden barrel filled with liquid. If an empty barrel is shot at, the ball passes through, making simply two orifices; if, however, the barrel is full of water, the energy transmitted to the incompressible liquid causes disruption and bursting of the constituent parts. This conception unquestionably contains a grain of truth and accounts for certain phenomena. But there is here no more than an accessory condition; the real cause of the commotion caused by the projectiles depends upon their great velocity. The terrible effects of the arms of war are thus explained.

The great revolution in military art by the introduction of organic explosives and powders has led to the transformation of armament and

to the utilization of projectiles of small calibre. The ball of the Chasse-pot and Gras rifles, which was formerly 11 millimetres in diameter, has been reduced to 8 millimetres; its weight also has been decreased from 25 to 15 grammes. On the other hand, the velocity has been increased. Instead of 450 metres the Lebel ball travels with an initial velocity of 631 metres per second. The rotary motion, which formerly amounted to 800 turns per second, is now 2,550. Since force depends upon velocity far more than upon weight, it will readily be understood that the Lebel ball, projected with a greater force, should be more effective. Its power is stated as 344.192 kilogrammetres, whereas in the Gras rifle it did not exceed 257.175 kilogrammetres. The truly active work accomplished—i. e., the coefficient of pressure per square millimetre—is three times greater: from 2.61 kilogrammetres it is raised to 6.847.

Country.	Model of rifle.	Calibre.	Weight of bullet.	Length of bullet.	Sheath of bullet.	Speed at 25 m.
		mm.	grammes.	mm.		metres.
France.....	1886	8	15	30	German silver.	600
Germany ..	Mauser-Mannlicher (1888)	7.9	14.7	31.6	Steel covered with German silver.	620
England...	Lee-Medfort (1889).	7.7	14	31.6	Id.	625
Austria....	Mannlicher (1888).	8	15.8	31.8	Id.	620
Roumania..	Mannlicher (1892).	6.5	10.3	31.4	Steel covered with nickel.	700
Russia.....	1891	7.62	13.86	30.48	German silver.	615
Switzerland	Ruhin-Schmidt (1889)	7.5	13.7	20	Copper.	600

The great velocity of projectiles and the reduction of their calibre have necessitated a change in their construction. In order to avoid the fouling of the barrel of rifles with lead and to prevent alteration in their form, and also to assure greater penetration, it has been found neces-sary to use projectiles having a nucleus of lead guarded by a layer of German silver. They are ogival cylinders measuring 30 millimetres in length; the anterior part, instead of tapering, bears the letter S.

The various European countries have modified their armaments in the same direction as has France. The question having a certain amount of real interest, we present in tabular form on this page the particular features of the principal models. It will be seen that the differences are, on the whole, of little importance.

The new projectiles were first experimented upon by Bruns, and later by Habart and Reger. These observers employed reduced charges and shot at cadavers placed at limited distances. They found that the pro-jectiles passed through the tissues and bone without being distorted or divided, and they never remained in the wound. They were, in fact, ideal projectiles of war; there seemed nothing to be done except to

arrest bleeding and to close the wound, since there were no foreign bodies or splinters to be looked for.

However, the researches of Chauvel and Nimier, Delorme and Chavasse, and Bogdanick led to less optimistic conclusions. The brilliant work of Demosthen conclusively established that the new projectiles are capable of producing fearful injuries, and his views were confirmed by von Coler and Schjerning, and by Labat.

The difference in results is due to the fact that the first experimenters employed reduced charges. They were thus able to fix at will the speed of projection; but in reducing the charge they diminished the speed of rotation. Now, the latter remains almost constant throughout the entire flight of the projectile; it is decreased hardly any with distance. It is to this factor, therefore, that the injuries produced by the new firearms are largely to be attributed.

Experimenting under actual conditions, it was recognised that, contrary to the assertions of several authorities, the new projectiles were easily distorted and fractured. Delorme and Chavasse admit the following classification in this respect: deformation of the point, lateral deformation, partial separation of the envelope, fragmentation with separation of the lead nucleus and of the envelope. These alterations may be produced on contact with bones, or when the ball rolls over after having struck a resistant plane, such as a gun, a piece of equipment, a carriage, or a wall. Thus deformed, a ball causes considerable damage and often lodges in the wound.

Thus we find that all the lesions which the old arms produced are noted here. While the Chassepot projectiles cause no serious injury at 1,200 metres, the new projectiles are effective at more than 1,500 metres; at 2,000 metres their velocity is still 197 metres per second. In former days a ball exhausted its effects upon the object with which it came in contact. At the present day the projectile can penetrate six cadavers at the beginning of its flight; at 1,500 metres it retains sufficient force to penetrate one. Finally, as Demosthen has shown, the lesions produced are not merely perforations. In the cranium a genuine shattering of the bones is induced; in the bones of the limbs, even when the projectile is discharged at a distance of 1,500 metres, comminuted fractures with 15 to 20 fragments are observed. Along the track of the missile the muscles are contused and mixed with fragments of osseous substance. It may be added that osseous fragments, receiving a certain amount of energy from the ball, may inflict glancing blows to the tissues; that cleanly cut vessels bleed to an alarming extent. If we remember that the effects are always less marked on the cadaver than on the living body, we arrive at the conclusion that the new projectiles are capable of causing lesions incomparably more serious than

the older types. It is then sad irony to designate as humane projectiles those bullets whose field of action is of wider range and whose destructive power is so much more extensive!

Explosions.—It is useless to dwell upon the various conditions under which explosions take place. The ignition of illuminating gas, the bursting of a vapour or compressed-air engine, the explosion of fire damp, the ignition of substances employed in the industries or used for criminal purposes, such as fulminate of mercury, dynamite, picrate, acetylene, represent a series of well-known examples.

The accidents produced by explosives are more complex than those caused by projectiles. Aside from the mechanical effects, the increase of pressure and the modification of temperature are to be considered. In some instances the temperature reaches 2,000° C. In other instances—for example, when an apparatus containing compressed air explodes—there results such a degree of cold as to induce death of the integument by freezing. Moreover, certain gases are deleterious, and to their mechanical and physical effects is added toxic action.

The first result of an explosion is an increase of pressure. In the case of illuminating gas, a mixture with air of one sixth of its volume gives a pressure of 18 atmospheres in the open and 23 atmospheres in a closed room. With explosive substances the figures are far higher; fulminate of mercury exploded in its own volume gives a pressure of 18,750 kilogrammes to the square centimetre!

Under the influence of these enormous pressures, a person stationed within the dangerous zone is violently thrown and flattened against the walls. In order to avoid this accident in factories where explosives are handled, the shops are made of wood. In the event of an explosion, the feebly resistant walls give way, leaving a free passage for projected individuals. A second danger lies in the fall of walls and ceilings. But the most fearful accidents are those produced by dispersion of a multitude of small fragments of glass, wood, stone, and metal. Thrown with great force, these bodies, however minute, may cause terrible destruction. This is easily understood from the following two facts borrowed from Brouardel:

An explosion occurring in a shop in Béranger Street, where fulminate of mercury destined for the manufacture of children's toys was stored, destroyed fourteen lives. Among the victims was an individual whose abdomen and thorax were torn open; the intestines, lungs, and heart were as though they had been minced. These frightful lesions were simply due to the projection of pieces of pasteboard used in the manufacture of cartridges. The small foreign bodies had lacerated the viscera, and the force of penetration was such that several fragments had entered the vertebral column to a depth of 4 to 5 millimetres.

In the dynamite outrage which took place in the Boulevard Magenta, one of the victims received more than a thousand wounds produced by sand, splinters of glass, and wood. Some idea of the force acquired by the minutest objects is given by the fact that in this same explosion a glass candlestick was found perforated through and through by a match.

Finally, cartridges of dynamite sometimes explode in the hands of workmen in arsenals. In such instances the bones of the hand then act as so many projectiles which penetrate the abdomen or the thorax. In a case observed by Bouchard a finger nail was driven with sufficient force to penetrate the muscles of the thorax and pierce the lung.

The various objects thus thrown are generally soiled with microbes, which may give rise to fatal infection. Thus, the man referred to in connection with the Magenta outrage died from the infections which developed in his wounds.

Simple Contusions and Contused Wounds.—We now come to the consideration of the less terrible but more common agents of contusion. Let us note, for example, the effects produced by blows from a club, kicks of either man or animals, collapse of buildings, or falls.

There may result a simple contusion or a contused wound.

There is *contusion* when attrition of soft parts is produced without wound or fracture.

There is a *contused wound* when the soft parts are torn.

In bones, three kinds of fractures may be observed:

1. Fracture at the point of application of the cause. For instance, when a traumatism—a blow of a club or a kick of a horse—breaks the bone at the point where it is struck.

2. Fracture at a distance. Here a curvature of the bone occurs, which gives way at its point of least resistance.

3. Fracture by *contre-coup*. A blow on the top of the skull, for example, causes a fracture at the base.

These three varieties of fractures may be observed when an individual falls on his heels. According to a multitude of concomitant conditions, a fracture of the calcaneum or of the leg, of the body or neck of the femur, of the pelvis, the spine, or the base of the skull may occur.

If the wounding agent is less active it causes a simple fissure, at times but microscopic fissures. These lesions readily heal; but they may be followed by persistent pain, and even by the development of hyperostoses as a result of too active reparative processes (Gussenbauer).

When a contusing body acts on the viscera, the lesions produced vary according to the resistance offered by the latter. In the case of the brain, the tissue is often reduced to a pulp; in that of the liver or the

spleen, simple or radiate fissures are produced, which are capable of giving rise to profuse hemorrhages.

If the contusing agent strikes an organ provided with a thick capsule—e. g., the testicle—the effects differ. The experiments of Monod and Terrillon have shown that the testicle is capable of resisting great pressure. A force of 50 kilogrammes is required to burst its envelope, which then yields and ruptures abruptly.

Notwithstanding all the injury inflicted by contusing agents, in most instances they do no more than dissociate the cells without destroying them. For this reason the bruised tissues, if transplanted beneath the skin of an animal, may retain their vitality and be ingrafted. (Gussenbauer), and this also explains why repair is so easily effected.

When a hollow organ is subjected to slight contusion, nothing beyond simple ecchymosis or a slight attrition of the walls occurs. In severe cases a rupture may take place. This accident generally results from compression of the organ between the wounding agent and some resistant part of the body—viz., a part of the skeleton. The kick of a horse perforates the intestine by pushing this organ against the spine; it is this bone that produces the perforation. Likewise, in falls upon the perineum, rupture of the urethra is due to the pressure of the latter against the ischio-pubic branch of the pelvis.

Finally, if an organ full of liquid is contused, it bursts; such is particularly the case with the bladder.

Rupture of the blood vessels naturally gives rise to hemorrhages, which may occur either immediately or subsequently to the injury, in the form of simple ecchymoses or interstitial effusions; or they may take place inside of some visceral cavity. Interstitial hemorrhages, when profuse, give origin to genuine tumours—hematomata. These may be circumscribed or diffuse. While they are, as a rule, limited, they may subsequently increase in size. Moreover, they may often become the starting point of suppurations.

In addition to effusions of blood, those of serum and oil are to be mentioned; and if the traumatic focus communicates with the exterior or with a neighbouring organ, effusions of gas or organic liquids may occur.

The secondary effects of contusions will be studied in another chapter. These are sphacelus and inflammation of the focus, and in some instances the formation of emboli in the diseased tissues.

Commotion.—An interesting variety of contusion is represented by the phenomena described as commotion. Two principal varieties are admitted—cerebral and medullary commotion. They will be treated of in connection with nervous reactions. It may be noted here, however, that the effects are in some instances accounted for by mechan-

ical lesions. Under the influence of a blow dealt at the anterior part of the cranium, the cerebro-spinal fluid, being driven abruptly, produces sufficient lesions in the floor of the fourth ventricle to explain the symptoms.

COMPRESSION.—We have hitherto supposed that mechanical agents acted by sudden pressure, and that they were endowed with a great amount of energy. In other cases the morbific agent exerts a continuous pressure, tending to diminish the bulk of the organs and to prevent their free expansion. Such a condition is spoken of as compression.

Compression may be produced by tight clothing, notably by shoes. It is often connected with the occupation of the individual, and is then attended by friction. In other cases it may result from improper adjustment of a surgical apparatus, or the use of crutches, etc.

Compression may also result from the development or displacement of certain parts of the organism. The head of the fœtus, when it rests too long in the parturient canal, may compress the nerves of the pelvis or the walls of the utero-vaginal canal.

Fragments of splintered bone, effusion of blood, and tumours push away neighbouring parts and cause disturbances and alterations.

The simplest cases are those in which the epidermis is compressed and becomes the seat of callosities. If a mucous membrane is compressed in a marked and persistent manner the result is an ulceration which may terminate in necrosis, gangrene, or perforation. In the case of a vein, compression produces a stasis, which is compensated by the development of a collateral circulation. The collateral circulation, however, is at times insufficient, and, as a consequence, œdema or, in very rare cases, even gangrene may appear. The latter is a far more frequent complication in those instances in which ischæmia results from compression of an artery—a state highly favourable to the development of microbes.

Finally, compression may affect a nerve, as is sometimes the case where crutches are used. The same thing occurs when a person falls asleep while supporting his head with him arm. In this case the radial nerve is compressed by the head at the groove of torsion. Formication is first felt, then sensation diminishes and disappears, and finally movement becomes impossible. If compression has lasted but a short time the paralysis soon disappears, and sensation returns, preceded by quite painful formication.

It is of importance to know these facts. Paralysis of the radial nerve was formerly attributed to the action of cold. It was said to occur when a person slept in the open air or with the window open. Dr. Panas has justly opposed this view. He has pointed out that paral-

ysis does not attack the limb exposed to the air, but the one that is compressed by the head.

Compression of the viscera by external agents is more rarely observed. We need but mention the effects produced by too tight belts and, above all, by corsets, which give rise to deformities of the stomach and liver. At autopsies it is not rare to find upon the surface of these organs the furrows which plainly show the impression left by the ribs pressed inward by the corset. The corset is even believed to play a part in displacement of the kidney. Renal ectopy, which is observed chiefly in women, and nearly always upon the right side, is attributed to the action of the liver, which, being pushed by the corset, presses the kidney out of place.

MECHANICAL AGENTS ACTING BY DISTENTION

All those agents which we have thus far studied exert pressure. We shall presently consider those that act by distention.

Disregarding distention of the esophagus by a too bulky bolus of food, and the therapeutic procedure employed in the treatment of a stricture by abrupt or progressive dilatation, we see that mechanical agents may act in two ways: In some cases the individual is fixed and the wounding agent tends to distend and to tear off a part of his body; in other cases a part of the body is held motionless by the external agent and the individual causes distention by an abrupt movement. As principal illustrations it suffices here to refer to the severance of a limb from the body by a revolving wheel or a power belt or the jaws of an animal. There are instances on record in which limbs were torn off by the surgeon in the course of mechanical manœuvres for reducing a luxation.

When a limb is strongly stretched it becomes distended. The limit of extensibility being reached, a rupture is produced. The rupture, however, does not occur simultaneously in all the tissues. The skin, by virtue of its elasticity, is almost the last to yield, the nerve trunks alone resisting longer. Separation having been effected, the tendons remain attached to the part torn off, carrying at their free ends some fragments of the muscles into which they were inserted. The ligaments behave in a manner similar to the tendons and separate the apophysis to which they were fixed. The muscles rupture at varying heights. According to Polaillon, the extensibility is overcome and then the relaxed muscle is torn. The majority of surgeons, however, are of the opinion that rupture occurs in consequence of a reflex contraction—i. e., the muscle ruptures itself. In regard to the skeleton, rupture sometimes takes place by separation of articulations; at other times, especially when the cause has acted obliquely, a comminuted fracture is observed.

It is a remarkable fact that wounds produced by distentions are not, as a rule, very painful and do not cause profuse hemorrhages. The latter phenomenon is explained as follows: The arteries being strongly distended, the inner and middle tunics are the first to give way; the outer coat becomes elongated and narrow, and when it breaks it becomes twisted so as to obliterate the lumen of the vessel and prevent bleeding.

A most interesting observation in this connection is recorded by Morand: A man employed in a mill was caught by a power belt and his arm torn off. The enormous wound thus inflicted was attended by hardly any hemorrhage, so that he was able to walk to and consult a physician. He recovered in two months.

As already stated, nervous tissue resists to a high degree. In certain instances a severed limb is held only by the nerve trunks. The latter, before rupturing, admit of considerable elongation. The median and ulnar nerves may be stretched to an additional length of 15 to 20 centimetres. The results of Tillaux and Trombetta demonstrated the fact that very great force is required to rupture a nerve. On the cadaver it is possible to raise the entire body by pulling the sciatic. From 50 (Tillaux) to 84 kilogrammes (Trombetta) are required to cause rupture.

Even for less voluminous nerves considerable traction is requisite before rupture occurs—38 kilogrammes for the median, from 20 to 25 for the ulnar, and for a little filament like the supraorbital nerve 2.5 kilogrammes.

Rupture does not occur at the point of application of the force. It is generally produced at the points of flexion. In the sciatic, for example, it occurs behind the ischium. In some cases the roots themselves are torn and detached from the spinal cord.

Resistance and Reaction of the Organism

In studying the mechanical agents, two factors are always to be taken into account—namely, the action of the wounding body, the importance of which we have sufficiently shown, and the resistance of the organism, which will now be considered in a few words.

Since the human body is a nonhomogeneous structure susceptible to numerous reactions, and notably to muscular contractions, which modify the effects of resistance, the problem is quite a difficult one. There are, however, certain influences which have been well determined. One is the age of the subject. Under similar given conditions children resist better than adults, and the latter better than the aged. In children, very energetic causes are necessary to produce marked disturbances and fractures. The incomplete ossification and the flexibility

of the bones explain their great resistance, as evidenced by the fact that a child may fall from a very great height without harm. On the other hand, in the aged the bones are rarefied and brittle. They are affected by what is called osteoporosis, and on the slightest cause they break. An abrupt movement in bed may cause a fracture of the neck of the femur, or a paroxysm of coughing may provoke a fracture of the ribs.

The resistance of the blood vessels is no less variable. In women, the slightest shocks are often sufficient to give rise to ecchymoses. Certain subjects, affected by a morbid state called hemophilia, have very grave hemorrhages from the slightest abrasion. Finally, arteriosclerosis, by diminishing the elasticity of the arteries, favours their rupture. In this connection may be mentioned aortic insufficiency caused by a blow on the thorax; the sigmoid valves rupture because they were already diseased.

Such illustrations might easily be multiplied, but these are sufficient to indicate the influence exercised by previous organic lesions upon the effects of traumatic agents.

General Reactions.—In addition to local lesions, we must take into consideration the general manifestations occasioned by traumatism —namely, the various reactions in distant parts.

The question whether a traumatic lesion can give rise to fever has of late been a matter of much discussion. After numerous experimental researches, the question seems to have been solved in the affirmative. Aseptic fevers are slight and transitory. Whenever the febrile movement is continuous, we should always look for some complication of an infectious nature.

Wounds attended by great mortification of tissues and extensive contusion are especially liable to invasion by microbes. The clean-cut wounds—for example, those produced by sharp instruments—are less frequently subject to infection. This is not due to the fact that the bacteria do not contaminate them, but, on the contrary, the tissues possess sufficient vitality to oppose their development and prevent their multiplication.

In a great number of subjects traumatic lesions give rise to intense nervous reactions, agitations, and delirium, and when violent may bring about a very grave and often fatal morbid complication—namely, *nervous shock*. Aside from these transitory disturbances, a series of permanent affections may appear. Hysteria and, more rarely, chorea and paralysis agitans have been produced in predisposed subjects by even slight traumatism. These disorders of external origin, as has just been indicated, may be transmitted by heredity. In this connection nothing is more interesting than the classic experiment of Brown-Séquard. The great physiologist severed the sciatic nerve in a guinea

pig; this traumatism gave rise to epileptiform convulsions, which were transmitted to the offspring.

In certain cases traumatism may be followed by permanent disorders, especially when nerves are involved. We here refer to trophic disorders, such as keloids, periostoses, exostoses, glistening state of the skin, small ulcers called by W. Mitchell causalgia, or nervous disturbances, such as neuralgia and painful cicatrices. In other cases traumatism proves to be an occasional cause of morbid localizations. In consequence of a blow upon the toe a paroxysm of gout may be observed, or perhaps a microbic localization, or even the development of a neoplasm. Max Schuller's classical experiment is well known. He inoculated tuberculosis beneath the skin of a guinea pig. At the same time a traumatism was produced at the knee. The pathogenic agent migrated to the wounded joint, and there gave rise to the formation of white swelling—*tumor albus*. Such facts are daily observed in clinics. Tubercular arthritis and meningitis are often referable to traumatic causes. Perroud observed in the boatmen of the Rhône a unilateral tuberculosis, the localization of which is due to the fact that these men propel the boats by means of a long pole which they press against one of their clavicles.

Influence of Passive Movements.—We have hitherto supposed that mechanical agents tended to modify the situation of a part of our bodies. The result is a sort of conflict the consequences of which we have already considered. In many cases a mechanical agent displaces the subject entirely, and, by a movement passively transmitted, it carries him into space. If the displaced individual finds himself in a locality absolutely inclosed and endowed with uniform motion, and if all the surrounding objects move with him, he will not be conscious of movement and will not present any physiological or pathological reaction. In fact, it is easy to understand that we perceive our displacement through the changes occurring in our relations to the surrounding objects or our situation toward them.

When we undergo passive movement, a series of manifestations occur around us which, if slight, make us aware simply of our displacement; but when they are intense they give rise to pathological phenomena. The first of these consists in variations of the blood circulation. By virtue of centrifugal force the blood tends to move in a reverse order to the movement which we undergo. The changes occurring in the circulation can be perceived through the peculiar sensation which we experience when the movement suddenly ceases—for example, when a train suddenly stops under the influence of the air brake. No matter how perfectly the vehicle may be equipped with devices to avoid jarring, the adjustment is never so complete as to secure

us against all agitation. Here is a new cause of disturbance. Serious disorders may at last appear, as in the case with railroad employees, particularly engineers. However, the agitation may also produce some favourable results. Patients suffering from paralysis agitans have often been improved by travelling or riding in automobile carriages. Impressed with this fact, Charcot conceived the idea of applying agitation or commotion to the treatment of this neurosis.

It is a matter of common observation that great oscillations, even when rhythmical, may occasion nervous disturbances. Such is the case with the swing. The dizziness resulting from its use is due to numerous causes. At each oscillation the centrifugal force tends to modify the circulatory hydraulics; the resistance of the air produces excitation in the mucous membranes and the skin; the displacement of objects acts upon the organs of vision; and, lastly, changes in the fluid of the labyrinth take place which affect the semicircular canals. Since the observations of Flourens and Cyon, it is known that an important part is played by this portion of the internal ear in equilibration.

An analogous mechanism serves to explain one of the most interesting disturbances of this order—namely, seasickness. In this case, however, the phenomena are more complex, since they are of a combined nature. We must take into consideration the oscillations of the vessel from side to side as well as those from stem to stern, and, in the case of steamers, to these must be added the vibrations produced by the engines. The results are disturbances of a sensitivo-sensory nature, modifications of the circulation, and displacement of the abdominal viscera. It is to the latter factor that the majority of authors attribute the most important rôle in the production of the manifestations. The visual disturbances, secondary though they be, should not be ignored, for it is often possible to avoid seasickness by fixing the vision upon distant objects. Objects that are constantly in motion should not be looked at. It is a well-known fact that when at rest we may experience malaise and dizziness by simply fixing our eyes upon moving objects. This, however, is only an auxiliary cause, since an individual may suffer from seasickness while the eyes are closed, and, moreover, the blind are not exempt from it.

The influence of visual excitation upon the causation of dizziness is also made manifest when the gaze is fixed upon the water or ground over which we move while riding on a river boat, in a carriage, or train. Yet, contrary to what would naturally be expected, no dizziness is experienced during the ascent of a balloon, no matter from what point the aeronaut may look.

In conclusion, it should be borne in mind that mechanical agents

may serve to fix us in a determined position. They then oppose our movements, and thus cause death. When, for example, an individual is caught in the ruins of a building, the *débris* resting upon him prevents the movements of the thorax, and thus causes asphyxia. In other instances mechanical agents fix the body in such positions as to completely modify the circulation. The human subject bears these changes fairly well, and, except when the head is placed too low, the circulation is carried on in a normal manner. In animals adaptation is not so readily accomplished; an animal fixed vertically soon dies from cerebral anæmia, since the heart is unable to cope with gravity and to send to the nerve centres a sufficient amount of blood.

CHAPTER III

PHYSICAL AGENTS

Atmospheric pressure—Influence of its variations—Mountain sickness—Altitude
cure—Heat—Burns—Heat stroke and sunstroke—Cold—Frostbites—Light, its
local and general effects—Braidism—Sound—Electricity—Physiological action
of currents—Fulguration and sideration—Electrocution—Practical applica-
tions of electricity.

PHYSICAL agents represent different forms of energy; they are five
in number: atmospheric pressure, heat, light, sound, and electricity.

ATMOSPHERIC PRESSURE

The air exerts upon the earth a pressure of 1.03 kilogramme per
square centimetre, or a total pressure of 18,000 kilogrammes for the
human body. We are able to support this enormous pressure only
because it is distributed in a uniform manner.

The variations of atmospheric pressure can influence our state of
health. When they are large and abrupt, and especially when rapid
depressions of the barometer take place, nervous disturbances are ob-
served in certain subjects, constituting *barometric neurosis*. Doubtless
this expression is not perfect. Along with the variations of pressure,
there occur changes in temperature, in humidity, in the solar radiations,
and in the direction of winds which must play a part in the final
result. Nevertheless, the barometric disturbances are most easily ap-
preciable and have served to designate the morbid manifestations. The
same influences may intervene to modify the resistance of living beings
to infectious agents; they explain the development of seasonal maladies
and play an important part in what is called the *epidemic temperament*
(*le génie épidémique*).

In order to distinguish the influence of atmospheric pressure from
other factors, it is necessary to consider what takes place when climbing
a mountain or making a balloon ascent. Such a study has a double
interest: through the serious accidents which it brings to our knowl-
edge, it gives us an idea of the beneficial effects of a sojourn in high
regions and of the mechanism of altitude cures.

It is a well-known fact that during an ascent the pressure decreases. The following figures, taken from the remarkable work of Regnard, give an idea of the variation of pressure with altitude. The sea level, upon which there is a pressure of 76 centimetres of mercury, is taken as a standard.

	Barometric height.	Altitude (in metres).
The sea....................................	76	0
Orthez	75	105
Aigle-Bains................................	71	540
Chamounix.................................	67	1,050
St. Bernard	56	2,370
The observatory of Mont Blanc.............	42	4,810
The pass of Parang (the highest point habitually visited by man)....................	37	5,835
Mount Everest (the highest point of the globe)	24.8	8,840
The ascents of Crocé-Spinelli and Sivel......	26	8,600
The ascents of Glaisher	24.8	8,838

In ascending in the atmosphere a number of disturbances are experienced which may prove fatal.

It is an error to attribute these symptoms to modifications in the constitution of the atmosphere. Whatever the altitude, the composition of the air is always the same; it always consists of 21 parts of oxygen, 78.06 of nitrogen, and 0.94 of argon. By means of a balloon sound Cailletet, the aerophile, was able to collect a sample of air at a height of 15,500 metres. The anlysis made by Muntz and Schloesing, Jr., gave 20.79 parts of oxygen, 78.27 of nitrogen, 0.94 of argon, and 0.0033 of carbonic acid. The somewhat low figure for oxygen is explained by the conditions of the experiment—a small quantity of this gas was absorbed by the copper plugs and by the oxidizable grease used to facilitate their working.

The only modification of the air in high regions is a notable increase in ozone; and this possibly is the explanation of certain therapeutic effects. A recent analysis made by Maurice de Thierry makes the variations of this gas quite evident: At the same hour of the same day, air gathered at Paris yielded 2.3 milligrammes of ozone; at Chamounix (1,050 metres) it yielded 3.5 milligrammes; and, finally, at Grands Mulets, on the slope of Mont Blanc (3,020 metres), 9.4 milligrammes.

Since the variations in the chemical composition of the air do not explain the harmful effects of altitudes, let us consider other modifications which take place on mountains.

There is, in the first place, a fall in the temperature. It is regarded as a law that the temperature diminishes one degree centigrade for each rise of 160 metres, a figure which may be retained, although it may not

be very exact.   Cailletet's apparatus indicated, at a height of 15,500 metres, a temperature of — 60°, while the calculation gave — 83° C.

What is of greater importance from a medical standpoint is that the cold is quite tolerable in high regions.   This result is for the most part due to the action of the sun's rays, which strike more perpendicularly than on the plain; and this explains also the considerable differences which are obtained according as the temperature is taken in the shade or in the sun.   At Davos, for instance, which is situated at an altitude of 1,560 metres, and is a winter resort for many consumptives, it is not unusual to observe the thermometer stand at —5° C. in the shade and + 12° C. in the sun.   If the bulb be covered with blackened cotton, in order to prevent radiation, the thermometer records + 30° C.   There is then a difference of 35° C. between localities exposed to the sun and those lying in the shade.

The snow, however, does not melt, because the air does not grow warm and the rays of the sun are all reflected by the white surface, which acts as a perfect mirror.   The proof of this is that if the surface of the snow be covered with a black body, such as a simple dead leaf, the snow melts at that point, because a storing up of heat rays occurs there.   Our clothes play the same part; they retain the heat and prevent us from feeling the cold, even on the snow.

Again, another condition favourable to life without suffering in high regions is the absence of wind and humidity.

Mountain air is so dry that putrefaction does not occur.   In the Valais, for example, when it is desired to preserve eatables, they are exposed to the sun without being salted.   Desiccation is effected before putrefaction can set in.   At St. Bernard the corpses of men and animals never decay, and, as it is impossible to dig graves in the rocky soil where the monastery is situated, they are placed in a morgue, where they are preserved indefinitely.

The rarefaction of the air explains also a phenomenon which often causes irritation to patients—namely, the absence of noise.   No sound is heard among the mountains because the air is no longer dense enough to transmit it; this phenomenon makes so vivid an impression upon certain persons that it produces a deep feeling of sadness.

Let us now consider the therapeutic effects of altitudes, and let us first study the influence of moderate altitudes.

Suppose, for example, a man who undertakes to receive, for therapeutic purposes, an air cure on a mountain from 2,000 to 4,000 metres high.   What will be the results?   Having arrived at the locality where he is to stay, that man will pass through a first period, that of acclimation; he will first feel a warmth quite noticeable on his skin. . His lips will be redder than in the normal state and his conjunctivæ

flushed. For two or three days he will have insomnia; he will occasionally experience palpitation, dyspnœa, dizziness, and, more rarely, headache. The urine is dark, constipation is the rule, and, finally, from the start, appetite is increased.

These first phenomena last for a week. At the end of this period the man is acclimated. The external appearance is changed; the skin assumes a tan colour; the integuments and hair are so dry that pomatum or vaseline must be used. The appetite has further increased, as has also the muscular strength, and the longest walks do not produce fatigue.

When afterward he comes down to the plain the skin becomes warm, burning, it splits and peels, but the favourable manifestations persist; the strength and appetite remain increased, at least for some time.

Mountain Sickness.—If we consider the effects of great altitudes, we find a series of disturbances which are collectively called *mountain sickness*. It is frequent at an elevation of 3,000 metres, but at 4,000 it is almost unavoidable. But it does not occur equally in all countries; it is more common in the Alps than in the Andes and the Himalayas. In Mexico an ascent of 4,000 metres may be made without incurring any sickness. Jourdanet reports that in the Andes villages may be seen at heights greater than 3,000 metres. On the basis of these facts, it has been stated that the higher the zone of perpetual snow the slower are the symptoms. In fact, cold is one of the principal elements in the genesis of the disturbances.

All climbers are not equally subject to mountain sickness. Training and temperament must always be taken into account. The quicker the ascent the greater the risk of being affected. If the ascent is made slowly, by short stages, acclimation is more readily effected. By repeating the ascents, the climber becomes proof against symptoms which a beginner can seldom escape. It is, however, important to know that the experience of the same person may be quite different in two successive journeys. An explanation of this fact is often found in his physical condition. When the evening repast has been poorly digested; when the sleep has been insufficient, agitated, disturbed, or interrupted, mountain sickness is likely to occur. The guides are not deceived in that respect, and from the appearance of the climber they predict to him how he will come out of his excursion. Indeed, fatigue is one of the most important factors, and this explains why mountain sickness is more common among climbers than among aeronauts.

The symptoms characteristic of mountain sickness are quite analogous to those of seasickness. The first phenomenon is a feeling of general weakness; the person has pains in the lower extremities, especially in the knees; soon saliva comes in great abundance into the mouth;

then nausea is felt, followed by alimentary vomiting, and, in grave cases, bilious and hemorrhagic vomiting. At a more advanced stage, the person has colic and diarrhœa; at the same time his body becomes covered with cold sweat. If he is examined at this moment his respiration is found to be very rapid, and the pulse irregular, rapid, and feeble.

If the person continues his ascent, he feels worse; dizziness, dazzling, humming in the ears, and a violent headache supervene. He falls into a state of indifference, an absolute apathy. He asks to be left undisturbed; he is not able to walk, his will is completely annihilated. He can not resist an invincible desire to fall asleep. In serious cases all movement soon becomes impossible, and profound exhaustion is produced, which terminates in death.

Many hypotheses have been proposed to account for mountain sickness; it has been attributed to the changes in the constitution of the air, but we have seen that this explanation is contrary to the facts; and it has been ascribed to an action comparable to that of cupping, which is also absolutely untrue.

The true theory, or at least the one that is to-day generally accepted as true, was put forward by Jourdanet and advocated by Paul Bert and by Regnard. According to these authors, mountain sickness is due simply to the rarefaction of the air—that is, the diminution of oxygen. There is, according to Jourdanet's expression, a *barometric disoxygenation.* Paul Bert made several very important experiments on this subject. He first submitted to analysis the blood taken from animals which had been kept in rarefied air. He observed that the quantity of the oxygen in the blood diminishes as the atmospheric pressure is lessened. If the rarefaction corresponds to the pressure existing at 2,000 metres of altitude, the oxygen diminishes 13 per cent; at 3,000, 21 per cent; at 6,500, 43 per cent; and at 8,500, 50 per cent. It is this lack of oxygen that causes death. In fact, if, as the air is rarefied, the proportion of oxygen in it be increased, the animal does not succumb; it does live at a low pressure, provided the air be supplied with a sufficient amount of oxygen.

Starting from this principle, Paul Bert experimented upon himself. He inclosed himself in a large bell in company with a bird and a rat. The air was gradually rarefied; the pressure fell to 24 centimetres, realizing the condition at the highest summit of the globe, at a height of 8,800 metres. Under these conditions the bird and the rat succumbed. Paul Bert himself was allowed, by a special contrivance, to breathe superoxygenated air; in that way he experienced no disturbance, but as soon as he tried to breathe the rarefied air in the bell, symptoms were manifested which disappeared under the influence of · oxygen.

Crocé-Spinelli, who witnessed the experiment, hoped to profit by it. In a balloon ascent which he made a few days later with Sivel he rose to a height of 8,600 metres. The aeronauts had taken with them receivers full of oxygen, but when about to make use of them, paralyzed by the cold and exhausted by altitude sickness, they were unable to reach their apparatus, and succumbed under the same conditions of aeration as those under which Paul Bert had survived.

The theory just expounded explains perfectly why one can resist better in making a balloon ascent than in climbing up a mountain; for in the latter case the muscular exertion, which is inevitable, requires the consumption of a considerable amount of oxygen to provide for the more active oxidation; therefore the effects produced by the diminution of this gas are felt much more rapidly.

Along with this principal factor we must take into consideration certain other conditions. The surrounding air being rarefied, intestinal gases expand and produce tympanites. At the same time the blood rushes toward the skin, and from this results anæmia of the internal organs. But it is quite certain that these diverse disorders play an altogether accessory part.

Acclimation and Altitude Cure.—When a person remains for a while on the mountains, three kinds of modifications take place in his blood; an increase in the capacity for absorbing oxygen, an increase in the number of red corpuscles, and an increase in the iron content.

Among the experiments upon which the foregoing conclusions are based we must cite those of M. Muntz, who operated on rabbits of the same brood, some of which had been left on the plain and others transported to the mountain, to the Pic du Midi. At the end of seven years, M. Muntz analyzed the blood of these two classes of animals, or rather of their descendants. M. Regnard made a similar experiment on guinea pigs. Instead of transporting some of them to a mountain, however, he made them live in rarefied air having the same pressure as at an elevation of 3,000 metres; the experiment lasted one month. Finally, M. Viault applied himself to the study of the red corpuscles, which he counted in the animals which had been transported, like those of Muntz, to the Pic du Midi.

Here are the results obtained:

	Oxygen absorbed in 100 grammes of blood.		Iron contained in 100 grammes of blood.	Corpuscles in 1 cubic milligramme of blood.
	Cubic centimetres.		Milligrammes.	
	Muntz.	Regnard.	Muntz.	Viault.
Animals { In the plain	9.56	14	40.5	4,000,000 to 5,000,000
{ On the heights..	17.28	21	70.2	6,000,000 to 7,000,000

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These figures, which are in satisfactory agreement, possess great practical interest and fully justify the use of altitude cures for those suffering from anæmia, and especially chlorosis. A sojourn in the mountains is the best means of modifying the blood, increasing its richness in red corpuscles and iron, and heightening its power of oxidation.

Increase of Pressure.—Like the diminutions, the increases in pressure are an interesting subject to study, on account of the symptoms they cause and the therapeutic effects they produce. Workmen who labour under water, whether for the purpose of gathering sponges, pearls, or corals, or laying the foundation of a bridge, find themselves in receivers in which the air is compressed to two or sometimes three atmospheres. The first phenomena consist of buzzing in the ears, due to the difference of pressure between the two surfaces of the tympanum; in the cavity of the tympanum the air but slowly attains the same pressure as in the exterior. The difference may be sufficiently great to cause rupture of the membrane of the tympanum; therefore individuals who have a catarrh in the Eustachian tube should be cautioned against remaining in compressed air.

At the same time a slackening and sometimes an irregularity in the respiratory movements are observed. The pulse, at first rapid, grows slow. Finally, the urinary secretion is notably increased.

All these phenomena are on the whole quite harmless. The grave symptoms occur at the moment when pressure is removed; the more rapidly this is done the more frequent the manifestations become. When these appear it is sufficient, in order to stop them, to compress some more air into the receiver, and afterward to reduce the pressure gradually. The pressure at the outside diminishing, while it remains increased in the cavity of the tympanum, it is readily understood that, by a mechanism diametrically opposed, auditory disorders occur as before. The person experiences buzzing in the ear; in certain cases the symptoms go further: hemorrhage results and the membrane of the tympanum may rupture. At other times the subjects complain of great fatigue and a tendency to fainting. If the reduction of the pressure is rapid, blood flows from the nose, ears, and lungs. On the skin, little punctiform hemorrhages will develop, which workmen designate under the expressive term of flea bites (puces). In serious cases paralysis may be observed, which generally attacks the lower extremities, often reaching the bladder and rectum, and which, if it lasts over forty-eight hours, may be regarded as almost incurable. Finally, a still more rapid reduction of the pressure may cause sudden death.

These various phenomena are readily explained on making an autopsy. All the vessels are filled with gas bubbles, because during

compression the nitrogen is in great quantity dissolved in the blood; on reduction of the pressure, if effected slowly, the nitrogen is gradually eliminated by the lungs; if the pressure be reduced rapidly, the abrupt changes in external pressure cause the liberation of the gas, the bubbles of which obstruct the vessels and arrest the operation of the heart, lungs, brain, medulla, and the pons.

The great variations of pressure occurring in case of explosion explain certain mechanical phenomena, and particularly the projection of small objects which, by their kinetic energy, cause more serious accidents. The increase of pressure, which sometimes does not exceed 20 atmospheres, may reach 1,500. But at the moment explosion takes place it first makes a depression that is an almost absolute vacuum around the victims; this is why they are shorn of their clothes. The air gathered between the clothes and the body expands and tears the clothes to pieces. Only such articles as shoes, garters, and corsets, which stick close to the body, may remain.

HEAT

Heat may act on the entire person, or on a portion of the body, in which latter case it may cause a burn.

In a general way, we may say that heat is not so well endured as cold. It is sufficient that the surrounding temperature rise to 40° C. for us to feel uncomfortable; we suffer from this temperature, which is 3° above that of our bodies; while the low temperatures of — 10° C. and — 15° C.—that is, from 47° to 52° below the temperature of our bodies—produce no inconvenience.

It is true that life may be maintained in countries where the temperature reaches, as in Senegal, 50° or 53° C., but it must be acknowledged that acclimation is there quite difficult. The majority of Europeans who emigrate to those regions succumb; their children pine and the race becomes extinct. On the contrary, in the case of emigration to cold countries, the organism easily adapts itself to the new conditions.

The differences are similar when we consider the variations of animal heat. When our bodily temperature rises 4° or 5° C., the situation is regarded as very serious, and survival is quite exceptional after 43° in the rectum is reached. Diminution of temperature is, on the contrary, much better endured, and it has been observed that animals readily recover after their temperature has been reduced, by abstraction of heat, to 20° and even 16° C.

We are not to believe, however, that we are unable to stand heat at a high temperature. It is possible to live in places having a temperature of 100° C. Blagden entered an oven showing 129° C., and staid there nine minutes.

The organism is able to resist these high temperatures because it possesses several means of protection.

In the first place, internal combustion diminishes. Then the vessels dilate, and the blood rushes to the surface of the skin, and this facilitates the loss of heat. Finally, and this third mode of resistance is the most important, sweating sets in and the evaporation of the secreted liquid produces a notable cooling effect. This is why dry heat can be endured much better than humid heat.

In those animals which do not perspire, such as the dog, evaporation takes place through the mouth; the animal puts out its tongue and executes rapid respiratory movements. If, as was done by Richet, the evaporation of the liquid is prevented by tightly muzzling the mouth, the animal succumbs to heat stroke; but the control, which breathes freely, resists.

For a systematic study of heat, we must successively consider its local and general effects.

Burns.—The local effects of heat are called burns and scalds. These may be produced by radiation, as is occasionally observed in certain trades, among glass blowers, for example. More often they are produced by contact with a hot body, liquid or solid. If it is a gas, the burns are superficial but extensive, and we shall presently see that the extent is of greater consequence than the depth. If it is a liquid, the scalds are deeper. Their extent varies according to circumstances. They may affect the entire skin of a person who falls into a vat of boiling liquid. A circumstance often increasing the seriousness of these scalds is that the clothes are impregnated with the burning liquid and prolong the action. In certain cases the phenomena of calefaction hinder the action of the liquid body; hence the possibility of plunging the hand or the arm, without inconvenience, into molten metal at a temperature of 1,000° C.

The burns produced by solid bodies are, in general, very deep, but limited, and consequently less serious.

In order to have an accurate idea of the effects of burns, we shall recall the well-known experiments of Cohnheim. This author plunged the ear of a rabbit into hot water. He states that a temperature of 42° or 44° C. produces but a transitory hyperæmia. At 48° or 49° C., the ear tumefies; œdema is produced. At 50° to 52° C., from the effusion of serum beneath the cuticle, blisters appear. At 56° to 60° C., gangrene of the ear sets in. Similar results are observed in man and allow us to separate burns into a certain number of categories or degrees.

It is usual, since Dupuytren, to admit six degrees of burns.

The first degree is erythema; this is a simple redness of the skin, produced under the influence of the radiant heat of a gas, of a liquid,

or of a solid whose temperature is not very high. In certain workmen, in glass blowers, for example, the erythema may assume a chronic character; the skin thickens and splits on the face and hands.

In the second degree the skin rises in blisters filled with serum.

In both cases the lesions are superficial; they usually heal without leaving any traces. Nevertheless, especially as a result of blisters, a certain indelible pigmentation may persist.

The remaining four degrees differ from the preceding in that they are attended by the destruction of the parts and give rise to the formation of cicatrices.

In the third degree the epidermis is disorganized and the mucous layer of Malpighi is reached.

In the fourth degree the destruction of the skin is complete.

In the fifth degree black masses are formed, involving soft parts to a greater or less depth. Finally, the sixth degree is reached, when the whole thickness of a limb is carbonized.

The extent is of far greater importance than the depth. If limited, a burn of the fourth, or even of the fifth degree is not serious; while a burn or a scald of the first degree may be fatal if it covers the entire skin. A person who falls into a vat of hot water and is immediately drawn out presents cutaneous lesions in appearance harmless, but he will succumb from the development of general manifestations. These differ entirely in their mechanism and symptoms, according as they appear soon after the accident or tardily.

The immediate general phenomena are manifested in the following manner:

There is, in the first place, a rise of temperature, which is explained by the application of heat; then, little by little, the temperature descends, falls below the normal, and may become very low. The respiration is slow, superficial, irregular, often intermittent with long pauses. The pulse is small, feeble, slow. Finally, the victim, indifferent to everything, falls into a comatose state, and succumbs with a progressive depression of the temperature.

These immediate consequences are observed especially in cases of extensive and superficial burns. The remote phenomena are met with when the lesions are deep.

The urine contains hemoglobin as the result of the breaking up of the red corpuscles. Sometimes hemorrhages occur, which are especially marked in the intestines and lungs. At the autopsy, nephritis and duodenal ulcerations are found, the former of which, at least, suffices to account for death.

The early symptoms are reflex manifestations, produced by the too violent excitation of the nerve endings; it is a variety of nervous shock.

The evils arising later are due to self-poisoning; there is an insufficient depuration in consequence of the suppression of the cutaneous emunctory and the increase of autogenous poison.   Experiments have demonstrated that burned tissues are very poisonous.

In a great many cases skin burns are accompanied by burns of the mucous membranes; these are due, in general, to the direct inhalation of flames, or may be caused by the ingestion of boiling liquids, as is the case with English children, who very often burn the mucous membranes of their throat and larynx by imbibing hot tea from the spout of the teapot.   The results are the same as those observed on the skin, except that the effects are much more serious, for the resulting œdema impedes the play of the organs, and, if the patient does not succumb, the consequent scars may ultimately cause strictures in certain passages, particularly the esophagus.

In cases of fire, the phenomena are more complex.   For we must first take note of the great quantity of gas produced.   It has been calculated that 1 kilogramme of burning wood suddenly yields by a silent explosion 200 litres of gas, which, under the influence of heat, expands to 10,000 or 20,000 litres.   The temperature at this moment is very high; at the focus of the conflagration it is not rare to find 1,000° to 2,000° C.

Death may be due to poisoning by gases produced, and particularly by carbonic oxide, which, causing asthenia or paralysis, prevents the victims from escaping.   At the autopsy the blood is found to be bright in colour, and it can be shown by the spectroscope that the hemoglobin is no longer reducible by sulphhydrate of ammonia.

In those who succumb under the influence of heat are found, besides burns of the skin, intrapulmonary coagula, appearing in the form of small casts.   When the temperature is very high the thoracic cavity is largely open, by a clean cut, as if by a cutting instrument.   The heart is hard, rigid, containing coagulated and dark blood.

With these great burns caused by fire we may parallel those produced in explosions of fire damp.   The lesions reach the respiratory mucous membrane and are explained by the following mechanism: The fire damp, mixed with the air which the miner breathes, fills his lungs; the external explosion propagates itself to the interior of the respiratory apparatus and produces burns in the trachea and bronchi, ecchymoses, and pulmonary hemorrhages.

In mines where there is no fire damp there may be observed, as Riembault has shown, a sudden deflagration of coal dust, which flies in the air and fills the respiratory passages; in this case also internal burns of a very serious nature are produced.

Heat Stroke; Sunstroke.—Besides its local action, the heat may give rise to a series of general manifestations which constitute heat stroke; this may be compared to sunstroke.

Heat stroke is most frequently observed in those workmen who labour in overheated places, among glass blowers, foundrymen, firemen, and particularly those employed in the firerooms of steamships. In the Red Sea, which lies between abrupt mountains, the heat of the climate, added to that of the engine, intensifies the symptoms to such a degree that it has been necessary to replace European by negro firemen, who can better resist high temperatures.

The sun claims numerous victims even in our own country. During the summer, cases of sunstroke are often observed among harvestmen, especially when they sleep in the sun. But it is soldiers that are most frequently affected. To the action of heat is added that of fatigue; hence accidents are much more frequent among the infantry than the cavalrymen, and occur mostly on the occasion of great manœuvres or reviews.

We must note also the humidity of the air in order to take into account its effects. Dry heat is, as already stated, far more easily resisted. Lastly, we must not forget that the most serious accidents occur when the heat or the sun acts upon the head. This is a fact of observation confirmed by experiment. By circulating hot water through a rubber bag Dr. Vallin was not able to produce symptoms except when he applied the apparatus to the heads of the dogs under experiment. We must also take into account our clothes, which may store up heat. After an hour's promenade in Paris, in the month of July, on a very sunny day, Vallin found under his hat a temperature of 46° C. At the end of a review in the sun the helmets of cavalrymen are often hot enough to burn the hand.

With a view of better analyzing the symptoms of heat stroke, Vallin subjected dogs to the action of the sun. The symptoms manifested themselves in three periods. At first the animal struggled and ejected saliva abundantly (it is known that the dog does not perspire); the temperature of the rectum rose from 39.5° (the normal temperature of dogs) to 42° or 43° C. Respiration reached the high rate of 200 per minute. In the second period the breathing became slow—it fell to 80 or 60; the agitation was followed by a complete prostration. The third period was characterized by convulsions, which terminated in death; at this moment the temperature of the rectum reached 44° or 46° C.

With man the evolution is less clear. We may, with Dr. Lacassagne, admit three periods. The first period, the least serious, is announced by certain premonitory symptoms—uneasiness, feebleness, heaviness in

the limbs. If the sufferer rests, all these symptoms disappear; if he continues to walk and expose himself to the heat, the lower extremities grow weak; respiration becomes difficult, dyspnoic; the thorax aches; the face is flushed; the cutaneous vessels become turgid. This is the asphyxial form.

In other instances, always in the first degree, the heat affects the circulation and gives rise to a syncopal form. The onset is abrupt; in the midst of a conversation, for example, the person is suddenly attacked; the face is deadly pale.

As a rule, the first degree is not serious; as soon as the patient is put in a cool place the symptoms disappear.

The essential characteristic of the second degree is the addition of nervous phenomena; there are dizziness and delirium; finally, coma ensues, and in certain cases death.

The third degree is that which causes rapid or sudden death, and is particularly observed in tropical lands.

Recovery, even in slight cases, is not always complete. Various disorders may persist, notably neuralgia, headache, and sometimes sub-delirious ideas.

The prognosis of sunstroke changes totally with latitudes; in temperate countries recovery is the rule; in countries where the temperature rises over 40° C. two thirds of the persons affected succumb.

Several theories have been suggested to explain the mechanism of the symptoms. The first idea attributed them to the coagulation of the myosin, which is produced at 45° C., but at the autopsy the muscular tissue is found acid and rigid, and notably the heart is contracted and hard. This view, advocated by Vallin, is being abandoned. In fact, it is established that the muscles are able to stand heat much better than was believed. Atanasiu, Carvalho, and Richet injected into the veins or peritoneum of dogs salt water heated to 60° C. without producing any disturbance. This burning liquid is perfectly well borne by the tissues and the heart. Therefore, it is more just to ascribe the disorders to an action upon the nervous centres, which are, in fact, the most delicate parts of the organism, and hence also the first to feel the influence of a rise of temperature. This theory, developed by Drs. Laveran and Regnard, seems to harmonize more satisfactorily with clinical and experimental results.

COLD

Cold climates, as above stated, are much more healthful than warm climates. Explorers who have been in polar regions state that they stood without any suffering temperatures from 40° to 45° C. below zero, provided there was no wind. Life may be maintained at even much

lower temperatures: at — 60° and — 70° C. However, the facts should not be exaggerated. In Russia, for instance, about seven hundred persons perish yearly through cold.

All ages are not equally fitted to stand severe cold. The adult resists best. The aged, whose nutrition is weakened, need a warm temperature. Children are very quickly chilled, but their tissues stand very well the loss of heat, and they survive depressions of temperature to which an adult would have succumbed. M. Edwards exposed to cold newborn dogs; the central temperature fell to 14° and even 13° C.; the animals, on being warmed again in a slow and gradual manner, recovered.

Sensibility to cold is increased by all causes which weaken organic resistance. Misery, overwork, starvation, and depressing moral influences must be mentioned first. This is the reason why cold acts so dreadfully upon a routed army. During the retreat from Russia, of which Larrey and Desgenettes have left us such striking accounts, the greater part of the soldiers died from the cold; the army, which comprised 400,000 men at its departure, was reduced to 3,000 when it returned to Germany.

Even in warm countries symptoms may be produced by exposure to cold, at least during the night. This is what happened during the African wars. In 1870, on the other hand, the accidents were mostly due to local freezing.

Another agency which frequently co-operates with cold is alcohol. In cold countries the inhabitants, especially cabmen, are very often seen entering wine shops to warm themselves. If they consume hot infusions, as tea, they can resist the outer temperature more easily; but if they take alcoholic drinks, and particularly brandy, as they do in Russia, on going out to the street, they often suffer from serious disturbances, and sometimes fall dead.

In order to fully recognise the action of cold, we must also take into account the wind and the humidity. The wind aggravates the cold, for it drives away the warm air surrounding the body. The humidity increases the loss of heat. Finally, melting snow is borne with difficulty, for it absorbs a great quantity of heat.

Furthermore, daily observation establishes the fact that cooling, when it is gradual and not abrupt, is more easily endured. An experiment of Paul Bert evidences this fact. Fish die when they are transported, without any transition, from water at 28° C. to water at 12° C. The converse is also true, demonstrating the danger of rapid warming.

As in the case of heat, we shall successively consider the influence of the local and general action of cold.

The local action is utilized in therapeutics. When it is desired to make a small operation, the diseased part is cooled, either by a mixture of ice and salt or by a vaporization of chloride of ethyl or methyl; the skin becomes white, bloodless, and insensible. When the cold application is stopped, reactionary phenomena are produced; the skin becomes red, congested, and the sensibility is exaggerated. The same method is applied, as is known, in the treatment of neuralgia. The vaso-constrictive action of cold is also utilized for the purpose of arresting hemorrhages or soothing inflammatory phenomena.

Frostbite.—When the action of the cold is more intense or more prolonged it produces various manifestations known as frostbite. In the clinic three degrees are known.

In the first degree, there are erythema and rubefaction; sometimes the cutaneous irritation is sufficiently marked to produce, as a sequela, a durable pigmentation. Some examples of this have been observed as the result of the use of chloride of methyl. When the irritation is repeated, the skin thickens, remains red, and sometimes cracks. Such is the erythema pernio, popularly known as chilblain, and is particularly observed among lymphatic persons.

In the second degree, the skin is ulcerated. In the third, eschars are formed, entailing the loss of the affected parts. These destructive lesions are particularly frequent in thin and exposed regions: at the lobe of the ear, at the tip of the nose, and at the ends of the fingers.

The different lesions characterizing frostbite are due, for the most part, to reactions of great violence; they are not caused directly by the action of cold, but by secondary phenomena produced by this pathogenic agent. They may therefore be avoided by moderating the reactions. It is a well-known fact in northern countries that a person suffering from cold should not be brought into a hot room. Circulation must be restored in the affected parts by mechanical means—by hard rubbing, rubbing with snow being the preferable mode.

During the retreat from Russia a great number of soldiers succumbed to terrible symptoms when they were transported into warm rooms. The affected parts were tumefied, distended by a considerable amount of serum; there was a disengagement of gas; the skin, swollen, was sphacelated, and death ensued in a few hours.

The greater the intensity of cold suffered the more serious are its effects. Operating upon the ear of a rabbit, Cohnheim obtained the following results: A freezing mixture at $-3°$ or $-4°$ C. excites secondarily a transient hyperæmia; at $-7°$ or $-8°$ C. it causes œdema; at $-10°$ or $-12°$ C., swelling; at $-18°$ or $-20°$ C., gangrene.

The mechanism of the accidents just indicated is easy to understand. Under the influence of cold the circulation grows slow; then, if the

temperature of the tissues falls to —15° C., the blood and the lymph coagulate. The red corpuscles become indented, burst, and their contents are set free. The hemoglobin passes into the urine; the stroma forms little foreign bodies, which obstruct the vessels and become the starting points of thromboses. When reaction is produced, the blood returns in abundance, and, unable to pass through the obstructed vessels, it transudes through the walls, causing œdema, while the most peripheral parts, deprived of the nourishing juice, soon sphacelate.

If the person succumbs, the same lesions are found as in those who have been burned. They depend on the same mechanism—that is, on a self-poisoning by the altered and destroyed red blood corpuscles and cellular elements. They are expressed also by gastrointestinal ulcerations, congestion, and sometimes hemorrhages of the abdominal viscera, lungs, and nervous centres.

General Effects of Cold.—The general effects of cold are quite complex; we must discriminate between ailments produced by cold itself and those in which cold plays an auxiliary part.

The first phenomenon consists in a general weakness, a feeling of fatigue, and an irresistible tendency to sleep. During the retreat from Russia the soldiers used to pray to be allowed to rest and sleep a few minutes; and yet they could see that those of their comrades who fell asleep never woke up again!

This state of apathy is sometimes interrupted by cerebral derangements, delirium, or by epileptiform convulsions. As Brown-Séquard has shown, when the body temperature falls to 22° C. there is produced, probably by the paralysis of superior centres, a medullary excitation, which is expressed by an exaggeration of reflexes, just as in animals poisoned by strychnine.

At the start, the organism tries to struggle by means of a more active combustion; until 30° C. is reached the exhalation of carbonic acid is increased. But when the temperature falls below 26° C., the organism abandons itself; nutrition grows slow or is arrested; the exhalation of carbonic acid is reduced, or at least its formation diminishes, since the blood in the veins becomes red, sugar ceases to be consumed, and glycosuria sets in.

Still, in most cases, death does not result from arrest of general nutrition; it is due to arrest of the heart's action. This is a point to which Drs. Richet and Rondeau have called attention; they have shown that it is possible to revive beings apparently dead through cold if, even half an hour after the cessation of manifestations of life, artificial respiration be practised, provided, however, that this is prolonged for a while, often for a very long time. The practical importance of this demonstration is readily understood.

In cases which we have thus far studied cold did not act solely by producing a loss of heat; it caused at the same time an excitation of the nervous terminations. The phenomena are, in fact, very complex, for it is possible to inject into the veins large quantities of ice water without producing any symptoms. This experiment is the reverse of the one we have recalled with reference to heat. We may also introduce as much as 100 and 160 cubic centimetres of ice water per kilogramme without giving rise to any disorder. The internal temperature falls 2° to 5° C.; at the end of one or two hours it returns to the normal; then it rises from 1° to 1.5° C. above the initial figure. Thus is produced a reactionary hyperthermia, which is, however, transitory.

Intraperitoneal injections of ice water are equally well borne and produce no disorder, not even diarrhœa. On the contrary, in injecting the liquid by the central end of the carotid artery, we often see convulsions, nystagmus, and movements of rotation or *manège* supervene. This is because the icy liquid passes through the carotid and vertebral arteries, reaches the nervous centres, and gives rise to the formation of softening foci in the brain, the cerebellum, and the peduncles.

Whatever the mode of introduction, the ice water has never caused diarrhœa, pulmonary alterations, or urinary symptoms. These morbid symptoms are indeed often observed after an attack of cold. In this case, however, the cold does not produce simply a reduction of heat; it gives rise to extremely violent and sometimes rapidly fatal nervous excitations. A guinea pig plunged into water at 4° C., care being taken to keep the head in the air, ceases to breathe and succumbs within a few minutes. This result is important from a medico-legal standpoint. Some individuals have survived after having remained quite a long time under water, while others, brought out sooner to the air, could not be restored to life. The difference depends largely upon the temperature; if the liquid is not too cold, the subject breathes, water is introduced into his lungs, and he is asphyxiated. If, on the contrary, the water is intensely cold, a cardiac and respiratory syncope takes place and the water does not penetrate the bronchi. In the first instance the drowned person is blue; in the second he is white (white asphyxia of certain authors), and, if artificial respiration be practised, he survives even if he had remained in the water for ten or fifteen minutes.

In order to put a little system into our study, we shall divide the morbid occurrences occasioned by cold into *five* groups:

Cold may produce *painful* phenomena. In many cases, particularly with arthritic subjects, a simple draught of air causes a facial neuralgia, often accompanied by an outbreak of herpes. In other instances motor disorders are produced—for example, a facial, perhaps even a

radial paralysis, although in the latter case, as already stated, it is generally due to a process of compression. Finally, with certain persons, extended paralysis has been observed, assuming usually the form of paraplegia.

A second group of phenomena consists of reflex disorders affecting mostly the *vasomotor* system. It is admitted that cutaneous cooling, involving a contraction of the superficial vessels, produces as a compensation a congestion of the deeper organs. As an example, reference is made to the results discovered at the autopsy of alcoholics dead under the influence of cold; a very marked congestion is found, and sometimes hemorrhages in the brain and lungs. Even in such cases the phenomena are complex, and congestive manifestations may be regarded as secondary. In fact, it is a matter of frequent observation that cooling of the skin excites vaso-constriction in the deeper tissues. Frédéricq has given experimental proof of this. By submitting the cranial skin of a dog to cold, a vaso-constriction of the meningeal vessels is produced. The phenomenon is too rapid to be attributed possibly to a reduction of heat; it is a case of reflex action. On the ground of this result it may be questioned whether pulmonary congestion, which is attributed to cold, is not a secondary manifestation, preceded by an initial vaso-constriction. We shall return to this question when treating of infections and nervous reactions.

In the third group are ranged the *hypercrinic* phenomena. Watering of the eyes, nasal catarrh, polyuria, and diarrhœa represent the best-known manifestations.

The fourth group consists of those cases in which the cold serves as an auxiliary cause to an *infectious agent*; it diminishes our resistance, and thus favours the development of bacteria, which live on our bodies as simple parasites. Hence, exposure to cold may be followed by angina, laryngitis, or pneumonia. In other cases cold provokes a relapse; such is the case with a person who, recovering from erysipelas, leaves his room too soon and is again attacked by the disease. Finally, cold may cause the development of complications in the course of a pre-existing disease by provoking secondary infections in the respiratory passages.

The *last group*, the least well known, comprises those very curious cases in which the cold gives rise to an attack of gout, or to the reproduction of an ascites in cirrhotic subjects. Finally, though in a manner as yet unexplained, cold may cause also paroxysmal hemoglobinuria. With certain subjects the urine contains hemoglobin as soon as there is a cutaneous cooling, even over a limited region. The phenomenon may thus be provoked at will.

It is a remarkable fact that cold does not seem to act any longer after a certain limit. Pictet demonstrated that one may descend into

a well showing a temperature of —100° or —110° C., the head remaining out. After staying there ten minutes the appetite is strongly aroused and the previous dyspepsia is notably decreased.

Choisat and Cordes utilized this result in therapeutics, and Letulle and Ribard conceived the ingenious idea of treating the anorexia of consumptives by the aplication upon the abdomen of carbonic snow at about — 80° C. Let us remember also that Dr. d'Arsonval has shown that the finger can be dipped with impunity in liquid air, or some of it poured upon a mucous membrane. It is more than probable that still lower temperatures would be even better supported. The human body would become wholly diathermanous, and the radiations would traverse it without making any kind of impression upon it.

LIGHT

Light has a very marked influence on all living beings. It may sometimes become destructive; microbes perish under its influence. Most frequently its action appears by the very notable modifications of nutrition in plants as well as in animals.

In the higher animals it stimulates the nerve ends, thus enhancing the nutritive activity. From this results an increase of resistance to pathogenic causes, a more energetic working of the organs, a notable improvement in ideas and feelings. Joy and cheerfulness are proverbial in sunny countries.

Certain experiments were made confirming these data. Let us represent by 100 the carbonic acid exhaled through the skin and lungs by a person shut in darkness. If this man is brought to the light, keeping his eyes shaded, the quantity of carbonic acid exhaled rises to 112. If the light is brought to bear upon the eyes, carbonic acid rises to 114. If the light acts at the same time on the body and visual apparatus, the acid reaches 136—that is, an increase exceeding the sum of the two preceding partial results. This increase of carbonic acid obviously indicates a nutritive overactivity; it coincides with an elevation of the bodily temperature. The result is particularly evident in children; their temperature rises from 0.1° to 0.5° C. when they are brought from darkness into daylight.

Light may, however, produce certain disturbances. The solar rays, arriving directly or after being reflected upon surrounding objects, cause an erythema, sometimes accompanied by a slight elevation of the epidermis by serous liquid. Electric light gives rise to analogous effects.

In the south of France and in Spain a disease is observed—i. e., pellagra, which is characterized by a chronic erythema occupying the exposed parts. There has been a good deal of discussion concerning the pathogeny of this affection; it seems to be due to the co-operative action

of different causes. In fact, it is observed in persons who consume spoiled maize. The alimentary poisoning engenders various nervous ailments and serious manifestations of a general character; at the same time it diminishes the resistance of the skin to the action of the solar rays. The eruption does not appear over parts protected by the clothes.

The notion that the harmful effects of the sun may be avoided by protecting the skin by means of blue or black glasses is a familiar one. Freckles act in the same way; the solar erythema does not appear where freckles are present.

The mucous membranes are even more sensitive to the action of light than the skin. The blepharitis and ophthalmia which are observed in hot countries and in those lands where the sun strikes the eye after being reflected from snow are well-known proofs of the fact.

The pathogenic action is due to the chemical rays of the spectrum— namely, to the violet and ultraviolet rays. Dr. Bouchard has demonstrated this fact by causing a ray of sunlight decomposed by a prism to fall upon the skin of his arm; the erythema appeared only in those parts that were exposed to the chemical rays.

The light may also give rise to reflex phenomena. On passing from darkness to daylight one is seized with sneezing. By gazing at a luminous object for a long while an artificial slumber may be induced, known by the name *braidism,* in honour of the author who discovered this phenomenon. The subject under experiment is found sufficiently asleep to make it possible, without awakening him, to perform painful operations upon him. By this procedure, even animals, particularly pheasants, may be made to fall asleep.

If the light shine brightly, it may produce more complex phenomena in predisposed subjects. When a magnesium lamp is lighted, catalepsy is caused; the person remains motionless in the very situation which he occupied, no matter how fantastic. If the light is suddenly put out, catalepsy gives way to lethargy.

The action of light may be compared to that exerted by the Röntgen rays. Their prolonged application has caused skin lesions, simply erythematous in most cases, but sometimes liable to end in the formation of small eschars. At the same time modifications in the general nutrition are induced, which are perhaps the result of the excitation of nerve terminations in the skin. This is a process comparable with that known in therapeutics as revulsion, and explains the effects obtained by the use of cathodic rays in the treatment of certain diseases.

SOUND

The vibrations of sound sometimes produce intense mechanical lesions, even a perforation of the tympanum. More often they act

by reflex action and stimulate activity in the nerve centres. Nothing is more restful than the absence of noise in the country or in the mountains, at least for certain persons, for, in others, silence may engender sadness and melancholy.

Noises, if intense, may produce disturbances in the predisposed. At the strike of a gong, hysterical persons fall into catalepsy.

Finally, it has been thought that harmonious sounds might serve as therapeutic agents, and that music might be used in the treatment of certain diseases. It is well established that music exerts a considerable influence over the nervous system. Its action deserves to be studied anew.

ELECTRICITY

To appreciate the action of an electric current two factors must be considered: the energy of the current and the resistance of the bodies it traverses.

The unit of electric *resistance* is the *ohm*; it is the resistance of a cylindrical column of mercury, one metre long and one square millimetre in cross section, at a temperature of 0° C. The resistance of the human body is, on an average, 1,000 ohms; this figure is obviously subject to great variations. Moreover, it must be noted that the resistance is not always the same during the passage of the current, and that it diminishes as the electric energy is increased.

Again, the resistance varies according as the current passes by this or that part of the body. Stone finds that the resistance, which amounts to 939 ohms when the current passes from one foot to the other, falls to 905 when it passes from the hand to the foot.

The second factor to be taken into account is the *energy*. In order to make it clear we may represent the form of the current graphically.
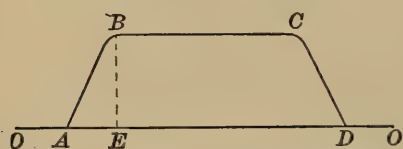

FIG. 1.—Electric wave, continuous current. $O\,O$, line of zero potential; $A\,B$, period of increase; $B\,C$, stationary period; $C\,D$, period of decrease: $B\,E$, measure of electric energy, difference of potential.

Let us suppose a continuous current passing in a nonelectrified body—viz., a body whose electric potential is equal to 0. We may distinguish in the electric wave (Fig. 1) three periods: a period of increase, a stationary period, and a period of decrease. The first and third periods, which correspond to the beginning and the end of the passage of the wave, constitute *variable states*; the stationary period is called the *permanent state*. Measuring by a perpendicular the distance which separates the permanent state from the line whence the current starts, we shall have the energy of the current; this is the difference of the

potential existing on the body considered before and during the passage of the wave, and if the useful effect is considered, it is called *electro-motive force*. The unit employed to measure electro-motive force is the *volt*; this is nearly the electro-motive force of a Daniell cell, which is taken as a standard on account of its great constancy. The ratio between the electro-motive force of a current and the resistance

of a body is called the *intensity* of the current. The formula $I = \dfrac{E}{R}$

allows us to determine easily this new unit, which is known as the *ampère*. The resistance of the human body being equal to 1,000 ohms, we must always, in our calculations, divide the number of volts by 1,000 to find the intensity. Consequently, it has been found simple in electro-physiology to measure by *milliampères*.

Let us return to the form of the current. Suppose the permanent state is suppressed; a single impulse (Fig. 2) will be obtained; this is what is realized in the electric spark, the discharge of a Leyden jar, and the lightning flash.

Again let us suppose that in a continuous current a series of breaks is made; then an interrupted current will be the result. But while
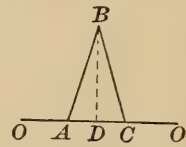

FIG. 2.—Electric impulse. *O O*, line of zero potential; *A B*, the period of increase; *B C*, period of decrease; no stationary period; *B D*, difference of potential.

continuous or interrupted currents are used they do not cause electrical effects only. Chemical effects are at the same time produced, owing to the electrolytic phenomena to which the current gives rise in the body, as in saline solutions. This chemical action may be suppressed by the use of alternate currents, the most important of which are the sinusoidal currents (Fig. 3). Each wave moves in a direction opposite to the preceding one; the successive figures are added, and, as they are in opposite directions, they neutralize each other. These currents therefore exercise a purely electrical action. The number of waves produced in one second is called *frequency*; double waves—i. e., two waves of opposite directions—are called *periods*. It is to be noted
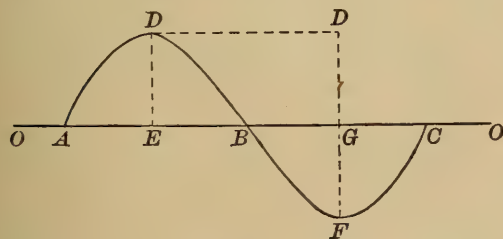

FIG. 3.—An alternating sinusoidal current. *O O*, line of zero potential; *A D B*, wave of positive electricity; *B F C*, a similar but negative wave; *A B* and *B C*, length of waves; *A C*, length of a period; *D E*, *F G*, difference of potential with reference to the line *O O*; *D F*, measure of "denivellation" of potential at each period.

that in currents of this kind the body at each period undergoes a diminution of potential equal to twice the energy of the current. If, for example, the current is one of 500 volts, the two successive waves

5

being of opposite directions, there would be between them a difference of potential of 1,000 volts.

We shall have finished these few preliminary remarks when we have added that the action of currents on the living organisms depends upon the form of the waves. When the waves are similar the effects are identical, whatever may be the electrical source.

If the organism is subjected to the action of a single wave, such as is realized in a lightning flash, sudden death may be the result, which is due to anatomical lesions and hemorrhages produced in the nerve centres, particularly in the medulla.

If the victim does not succumb, paralyses may persist, some of which are due to a material lesion, while others belong to the category of hysterical phenomena, called by Charcot *kerauno paralyses* (*keraunos*, lightning).

Continuous currents act upon the organism only when the potential is being modified; that is, during the variable periods—the closing or the break of the current. So long as the permanent state lasts no phenomena occur, excepting, of course, the disturbances due to electrolysis.

If an animal is subjected to the action of a continuous current of sufficiently high potential—for example, 400 volts—at the closing and opening of the current a muscular contraction is produced. If the shocks be repeated a great number of times the animal is killed. But, as d'Arsonval has shown, in such a case death is due to the large amount of heat generated by muscular work; for, if this experiment be repeated upon an animal plunged into a cold bath survival is the rule.

Very powerful continuous currents, amounting, for instance, to several thousands of volts, may produce a fatal shock. In the industries, continuous currents furnished by dynamos are much more dangerous than currents supplied by batteries; for the break currents give rise to phenomena of self-induction and to the production of extra currents which, if the voltage is high, produce sideration. A current short of 300 volts produces but one shock; between 300 and 1,000 volts it causes a very painful sensation; at 3,000 volts it may, though not always, entail death.

From a physiological standpoint the most interesting currents are the alternating currents, the effects of which were thoroughly studied by Tesla and d'Arsonval.

Let us suppose a sinusoidal alternating current having no chemical action; if the potential is low, and if the frequency is also low, the current produces no notable effect upon the human body; it modifies only the nutrition, as may be shown by analyzing the urine.

At a moderate potential and a moderate frequency the current produces a muscular contraction which is not painful.

If the potential is raised, and if the frequency is from 100 to 200 per second, sinusoidal currents give rise to serious and even fatal accidents. These currents have been most extensively utilized in industries and are also used in America for electrocution.

Let us now assume that the potential and the frequency are increased. The action will be more and more marked, and then, for an instant, the effects on the organism will no longer vary; beginning from 2,500 to 5,000 excitations per second, the manifestations diminish. When the frequency reaches several hundred millions or several billions, whatever be the voltage, the currents become harmless.

The following experiment, repeated a great many times in Professor d'Arsonval's laboratory, well illustrates this point. A steam engine furnished a current which was used for electric illumination and which accidentally caused the death of a man. This current, when transformed to an alternating sinusoidal current at high frequency, can harmlessly traverse the human body. Two men desire to be experimented upon; each one puts himself in contact with one of the poles. Then the two men are joined by a metallic conductor bearing six incandescent lamps; the six lamps are lighted, while the men do not experience the slightest sensation. And yet, if the frequency was diminished, the two persons would soon be killed.

To explain the innocuous character of high-frequency currents, Professor d'Arsonval has advanced two hypotheses. We may admit that the current has no power of penetration and that it simply glides over the surface of the body. On the other hand, we may suppose that the nervous system ceases to be influenced when electric vibrations become too frequent. In support of this conception the cases of light and of sound are recalled. The auditory nerve is impressed only when the waves have more than 30 and less than 30,000 vibrations per second. The retina perceives but those rays whose vibrations are comprised between 497,000,000,000 and 728,000,000,000 per second. Below or above these figures there is no stimulation. Why, then, should we not admit for electricity what is demonstrated for sound and light?

Currents of moderate frequency used in the industries have caused a number of accidents, many of which have been fatal.

But, in view of the extent which electrical industries have reached, we must recognise that the number of fatal cases is by no means very considerable. Biraud, in his excellent thesis, was not able to collect more than 10 such cases in France and 20 in England. In America, where the use of electricity is so extensive, he found only 200 cases.

In factories a number of precautions are observed which, if well

followed, would be entirely efficacious. Workmen must protect their hands by the use of rubber gloves. It is to be remembered, however, that the rubber, in getting old, may crack and let the electricity pass. Another precaution consists in not wearing shoes with nails, and in using rubber soles. This measure is excellent, for the most serious accidents have been those which are caused by currents passing from the hands to the earth. Finally, the tools are provided with insulating handles.

If, through neglect of these precautions, an accident happens, the effects vary according to the extent of the contact, the condition of the parts affected, and the position of the body with respect to the current.

It is quite evident, in the first place, that the more extended the contact, and the better conductors the parts through which the current enters or leaves, the more serious will be the injury. The humidity of the hands, for instance, favours considerably the penetration. But it is especially the position of the body with respect to the current that modifies the results.

Three events are possible. The two hands touch two points of a conducting wire, thus completing the circuit. The resistance of the body being higher than that of the wire, the effects will not in general be serious.

In other cases, the entire current passes through the body—for example, when a workman takes the two ends of a broken wire to mend them. If the current does not reach the ground, the effects are often almost harmless.

Finally, when the current reaches the ground, the phenomena of sideration supervene; currents of 2,000 volts may bring about death, while in the preceding cases currents of 3,000 volts caused some shaking.

The effects produced by currents may be divided into two groups. Some of them are local manifestations—burns which are more or less intense, according to the degree of resistance. They are therefore observed in relatively harmless cases, when, for example, very dry hands resist penetration. If, on the contrary, the hands are moist, they are good conductors and the phenomena of sideration are produced. These are very simple; the person falls as if struck by lightning and his respiration is arrested. Yet the accidents are not irremediable; it is only a case of apparent death, a variety of nervous shock, and if artificial respiration is practised for a sufficient length of time he is restored to life. But sometimes there occur irremediable hemorrhages in the nervous centres. These lesions, which were the rule in the case of fulguration, are rarer in sideration. This is one

difference between the two states. There is another difference. The kerauno paralyses of Charcot are observed only after fulguration; they do not appear after sideration.

Electrocution.—The idea of utilizing electricity in capital executions seems to belong to a French senator, but the experiments were made in America. Brown and Kenelly were asked to determine the fatal effects of the electric fluid on animals. They used currents of 200 to 280 alternations per second, and succeeded in killing a dog with 200 volts; 700 volts killed a horse.

The first experiment on a human being took place on August 6, 1890, in the prison at Auburn, N. Y. The condemned person was seated on a wooden chair and tied fast. A casque was put on the head and a wet sponge on the sacrum; the preparations took three minutes. Then a current of 2,376 volts was passed for seventeen seconds; the person seemed to be dead, but a few minutes afterward the pulse revived, and at the end of thirty seconds a slow movement of the thorax seemed to be noticeable. The current was again applied for seventy seconds, and this time he succumbed.

The following year, on the same day, there was occasion to make four capital executions. With the first condemned one, a current of 1,548 volts, passing from the head to the calf for 37 seconds, did not prove fatal, and a second contact of 36 seconds became necessary. For the three others, currents of 1,845 volts were used; for each one three successive contacts of from ten to eighteen seconds were required.

These results appeared excellent, and in 1892 it was considered proper to invite to the execution a number of persons, especially journalists. After a lecture delivered by the physician in charge of the operation, the condemned man was brought in. They dipped his hands in acidulated water, and, as a precaution, in case the new system should not succeed, the casque was applied to his head and the wet sponge to his calf. The current, of 1,600 volts, passed through the hands for fifty seconds. By this time the water had evaporated and the hands were carbonized. Yet the heart was beating; then the mouth opened and saliva was thrown out, certain movements were produced, and several spectators heard a groaning. Then the current was applied from the head to the calf for thirty seconds, and he succumbed.

At a subsequent execution it was decided to verify the value of artificial respiration, advocated by Professor d'Arsonval as a treatment of sideration. The experiment met with a marvellous success and saved the life of the condemned. This fact is obviously very important from a practical standpoint, and is perhaps the best result furnished thus far by electrocution.

Practical Applications of Electricity.—The practical medical applications of electricity are very numerous. It may be used for diagnostic as well as for therapeutic purposes. The study of electro-muscular contractility plays a very great part in nervous semeiology. Therapeutists use the electric fluid in all its forms, static electricity, continuous and broken currents, and currents at high frequency. It is particularly in nervous affections that electricity is of service; it is of real utility against paralyses and muscular atrophies; it is equally valuable in combatting tics, cramps, and neuralgia. It is used in cases of atony of organs supplied with unstriated muscular fibres. Many successes have been obtained even by the use of electrical baths in cases of intestinal occlusion.

Finally, whether by static electricity or by currents at high frequency, success in modifying nutrition or calming general disorders, such as those which characterize neurasthenia, has been obtained.

Electricity may also be used for producing electrolysis. When an electric current is passed through saline solutions it causes decomposition; the acids are attracted toward the positive pole and the bases toward the negative pole. The same phenomena occur in the organism, and have been turned to use in therapeutics. Electrolysis is employed to destroy certain pathological tissues. Although it has been abandoned in the treatment of aneurism, it is resorted to in the treatment of erectile tumours, uterine fibromata, and strictures of the urethra. It is also employed for destroying the hair.

A last application of electricity is the galvano-cautery; but in this case it is not the electric fluid itself that is concerned, but the heat which it develops.

CHAPTER IV.

CHEMICAL AGENTS

Caustics—The toxines—Exogenous poisons: alimentary poisons, air poisons, poison-
ing due to occupation—Criminal, suicidal, and accidental poisoning—Venoms
—Mode of penetration of poisons—Transformation, elimination, and accumu-
lation of poisons—The toxic equivalents: their variations—Habit—Anatomical
lesions of toxic origin.

In studying the physical agents we considered the contingent prop-
erties of bodies, those that are independent of their constitution. We
have viewed the world of energy. With the chemical agents we enter
the world of matter. We are now about to study those properties
which depend upon the molecular structure of bodies.

Chemical agents are divided into two groups: caustics and toxines.

Caustics

Caustics are bodies which, by virtue of their chemical affinities, are
capable of altering and destroying the living part with which they
come in contact.

The action of caustics is known as mortification; the result is
called eschar. Mortification is the more energetic the greater the
chemical affinity of the caustic for albuminoid substances.

The organism presents various means of protection against the
action of caustics. The skin is covered with a coating of grease,
which shields the subjacent stratified epithelium; this resists fairly
well. If it be reached, alkaline albuminoid secretions are produced
which neutralize certain substances and form insoluble combinations
with others.

Caustics were formerly divided into mild and escharotic or strong
caustics. To-day they are divided, according to Mialhe, into coagu-
lating and liquefying caustics.

Coagulating caustics are represented by metallic salts, acids, and
some essences.

Metallic salts, among which silver nitrate, acid nitrate of mer-
cury, and zinc chloride deserve especial mention, give rise to two types

of lesions. Applied to superficial parts, they cause instantaneous death of the cells—that is, mortification; they destroy them without modification of their normal histological characters. In the deeper tissues they produce fatty degeneration of the anatomical elements.

Acids, of which sulphuric, hydrochloric, nitric, and chromic are the most important, often produce very extensive eschars. Although their action is diminished by the water they absorb from the tissues and by their union with the alkaline fluids, the lesions caused by them are generally profound. The aspect varies according to the substance. The eschar produced by nitric acid is yellow, owing to the formation of xantho-proteic acid. Sulphuric acid produces black eschars, the colour being due to an alteration of the colouring matter of the blood and to the liberation of carbon contained in the cells.

Lastly, essences, notably those of cinnamon, bergamot, and meadow sweet, possess, according to Dr. Pilliet, the power of causing on the surface of mucous membranes lesions similar to those produced by sulphuric acid.

Liquefying caustics comprise the bases potash, soda, and ammonia, and an acid—arsenious acid. The bases act by dehydrating the tissues and forming soluble soaps by union with fatty substances, also by decomposing nitrogenous substances. The eschars are soft, and, on separating, leave the blood vessels exposed, frequently causing grave hemorrhages.

The cicatrices produced by various caustics are often severe, and may be followed by contractions interfering with motion. Functional troubles are particularly frequent when mucous membranes are involved. For example, strictures in the esophagus result, necessitating the establishment of a gastric fistula.

TOXINES

Many definitions of toxic substances have been given. Aside from those found in the codes, and which have no scientific value, we believe that a much broader meaning should be assigned to this term than is usually done. Therefore, we propose the following formula:

Toxines are those substances which, when introduced into or formed within the organism, are capable of disturbing or abolishing the life of anatomical elements by either directly or indirectly modifying the liquid medium containing them.

We include in this definition the very important group of toxic substances formed within the organism—the endogenous poisons—among which those concerned in auto-intoxication have been best studied. We repeat, that poisons act by disturbing the medium in which the anatomical elements live. This is a characteristic distin-

guishing the toxines from all other agents heretofore studied—in fact, all the others altered the parts with which they came in contact. Toxines, on the contrary, do not act until they have been absorbed, have penetrated into the blood and interstitial fluids, and have modified their chemical composition.

Our definition naturally leads to the division of the toxines into two groups: *exogenous,* altogether formed before their penetration into our organism; *endogenous,* which are generated within our own bodies.

Endogenous poisons are subdivided into *heterogenous* and *autogenous.* The former are produced by parasites or microbes accidentally or normally lodging in our bodies; the latter result from the very life of our cells. It is a general law that all living cells constantly produce substances which, if not eliminated on the one hand while formed on the other, derange and arrest the manifestations of life.

The following table will give an idea of this division:

$$\text{Poison} \begin{cases} \text{Exogenous} \begin{cases} \text{Habitual.} \\ \text{Accidental.} \end{cases} \\ \text{Endogenous} \begin{cases} \text{Heterogenous} \begin{cases} \text{Parasites.} \\ \text{Infectious agents.} \end{cases} \\ \text{Autogenous, by cellular life.} \end{cases} \end{cases}$$

Aside from the endogenous poisons, the history of which will be presented when treating of parasites, microbes, and nutritive disturbances, we shall consider exclusively the exogenous substances. We shall review in succession alimentary poisons, air poisons, poisoning due to occupation, accidental intoxications—whether criminal or voluntary—and conclude with the history of venoms.

Alimentary Poisons.—Among the common exogenous poisons are to be noted, first, the alimentary poisons, and chief of these the potash salts. These salts are useful, indispensable. Dogs fed on meat freed from potash salts succumb at the end of ten days—that is to say, much sooner than under the influence of absolute starvation. If great quantities are ingested, the excess is readily eliminated through the urine. But if the kidneys are altered, potassæmia results; and some authors hold that an accumulation of potash salts is responsible for the phenomena of uræmia.

Side by side with the potash salts are often placed the albuminoid substances contained in the tissues. It is certain that their intravenous injection speedily causes death. As a matter of fact, however, these substances are transformed into peptones in the digestive tract. The peptones, being dehydrated in their passage through the intestinal membranes, form new albumins adapted for the nourishment

of the cells. It may possibly happen that, in the case of certain lesions of the intestinal membranes, peptones penetrate as such into the organism; they are then found in the urine. There has been a great deal of discussion in reference to the toxicity of peptones. It would seem that, if not peptones, at least albumoses produce noxious effects; at all events, when injected into the veins, they can render the blood noncoagulable for several hours; at least, that is what occurs in the dog.

A last cause of habitual intoxication is represented by the putrefaction which occurs in the intestinal contents under the influence of microbes. We shall again refer to this when studying the bacterial agents.

ALCOHOLISM.—Toxic substances are found in beverages even more than in aliments. Water contains mineral salts, and, most important of all, the products of putrefaction of organic matter, which render it injurious.

At the present day plain water is seldom drunk; alcoholic beverages are largely consumed which, without exception, are toxic, and in certain doses may speedily cause death. One litre of rum is estimated to be a fatal dose for an adult. In children, serious accidents occur with far smaller doses. Taylor reports the case of a child of seven years who died from the effects produced by drinking 100 grammes of brandy.

We most frequently have to deal with chronic alcoholism. It is not necessary to state that this form of intoxication is steadily on the increase in the majority of countries. In 1830 France annually consumed a quantity of beverages corresponding to 1 litre of absolute alcohol per capita; in 1885 the consumption had risen to 3 litres, and in 1891 to 4 litres per capita. This figure is still below the actual consumption. This is established by official statistics, which give for each year and for all France 1,545,045 taxed hectolitres. The amount of alcohol passing fraudulently is estimated at 500,000 hectolitres. The annual consumption for each inhabitant may then be estimated at 5 litres, which correspond to 13 litres of brandy. Moreover, if we reflect that there are many who consume no alcohol and that children drink hardly any, we must acknowledge that the figures are very high.

Statistics further demonstrate the existence of a striking parallelism between the advance of alcoholism and the increase of insanity, suicides, and crime. We have said that alcoholism is on the increase in almost every country. In Denmark, the consumption of alcohol is 8 litres, and in Belgium 12 litres per capita. In some countries, owing to certain measures adopted, the advance of this evil is being checked. In the United States the consumption has fallen to 3 litres, and in

Norway, where alcohol once made fearful ravages, it does not exceed 2 litres per capita.

The universally used expression "alcoholism" is incorrect in that it takes the part for the whole; for in the so-called alcoholic beverages ethylic alcohol is certainly the least toxic ingredient. According to a law which offers very few exceptions, the toxicity of alcohols increases with their atomic weight. Alcohols of high atomicity—propylic, butylic, amylic, œnanthylic—which are met with in most beverages, and particularly in brandy, are far more noxious than the alcohol of wine.

Besides alcohols, we must mention aldehydes, and, among these, pyronic aldehyde or furfurol, all of which are convulsive poisons, and are found in vermouth and bitters. There are also ethers, acetone, various volatile bases, hydrocyanic acid, and, last but not least, essential oils. Absinthe contains nine different essences, all toxic substances.

We must make special mention of a product too often considered as inoffensive—namely, aqua melissæ. Women particularly make use and abuse of this preparation, which often gives rise to very grave disturbances, notably to paralysis, the nature of which is not always easily determined.

We may state in conclusion that alcoholism is a complex intoxication, hence the variability and multiplicity of the disturbances.

ACCIDENTAL ALIMENTARY POISONS.—In addition to the toxines which we ingest in consequence of our social habits, others exist which can be regarded as accidental. At the head of the list stands *lead.* Nearly all beverages, water not excepted, contain more or less considerable quantities of this metal. In cities the water pipes are of lead, and water dissolves traces of it. In this event danger is not great, as the lime salts contained in the water are deposited inside the pipes in such a manner as to form a sort of protective coating.

Lead is found especially in cistern water, which is pure and aerated, and in water containing organic substances in a state of decomposition. Although opposed to each other, these two conditions are most favourable for the solution of the metal.

In other cases lead comes from reservoirs painted with vermilion, from earthenware varnished with substances containing lead, and, in carbonic waters, from metallic vessels. According to Dr. Moissan, Seltzer water may contain as much as 0.9 milligramme of lead to the litre.

Alcoholic beverages especially are oftenest contaminated with lead. The different pieces of the retorts and presses may leave traces. Unscrupulous manufacturers add litharge to diminish the acidity of wine and cider, and acetate of lead to clarify beverages. We must also take

into account the grains of shot that may be left at the bottom of bottles after cleansing.

Aliments are no less contaminated. Take, for example, bread. The millstones present small holes which are filled with lead; the tubes which conduct the flour to the bolter contain some lead; in the bakery refuse wood painted with white lead is sometimes used for heating the ovens, which wood gives off small amounts of this metal under the influence of the heat. Among other aliments, butter coloured with chromate of lead may be mentioned, and also preserved game killed by leaden bullets. Preserves are worthy of particular attention. The pewter which is used to solder the boxes contains a considerable amount of lead, which is readily dissolved in preserves containing oil; in peas, only 2 milligrammes of lead are found to the kilogramme; in sardines, 40 to 50 milligrammes; in preserved beef, particularly in that intended for use at sea, Schutzenberger and Boutmy detected as much as 1.48 gramme per kilogramme. Most of the disturbances described as dry colic of hot countries have been shown by Amédée Lefèvre to be cases of lead poisoning.

Among other sources of saturnine intoxication we must note pottery, oilcloths, tinned utensils, the pewter foil surrounding chocolate and tea, the grinding machines of the butcher, the oilcloths painted with chromate of lead and used for packing ham and cheese, and nursing bottles with lead nipples.

This enumeration sufficiently establishes the fact that people ingest daily a certain amount of lead; consequently, traces of it are often found in the urine. Putnam was able to find some lead in 17 per cent of the healthy subjects he examined. In the sick the proportion is as high as 50 per cent.

Although the continual absorption of lead at times provokes gastrointestinal disturbances, indigestion, and colic, it most often causes chronic manifestations. Arteriosclerosis and interstitial nephritis, so frequently observed after a certain age, are very often the results of a slow and progressive intoxication by this metal.

Copper is perhaps as widely diffused as lead, but it is less dangerous. It is found in bread, and especially in wine, since *Bordeaux bouillie* has been employed instead of mildew. Wine, cider, and beer, even without the aid of heat, rapidly attack copper. Condiments prepared with vinegar and pickles always contain some. Some is also met with in vegetables, which, in fact, possess the property of taking up the metal contained in the soil; and notable quantities of it are found in the hulls of various grains.

It is easy to understand that copper might invade the organism of herbivorous animals from the vegetables eaten. That is why we find

some in the meat we consume. Dr. Gautier thinks that one can tolerate 18 to 20 milligrammes per kilo, but these quantities are often exceeded. As much as 200 or 210 milligrammes of copper salts may exist in one kilogramme of preserved substances.

It can be said, then, that we ingest some copper and lead every day. Dr. Gautier estimates the minimum at 1 to 7 milligrammes and the maximum at 20 to 30 milligrammes. These salts, however, are of little toxicity. Taken in large doses they are rejected by vomiting; in small doses they are well supported. Dr. Galippe has given some to dogs, and he himself, his family, and friends have ingested these substances during months and years without observing the least disturbance.

Another and far more toxic substance is *arsenic*, which is often found in wine. In 1881 four hundred persons were poisoned at Hyères and Havre by arsenical wines. Again, it is in preserves that arsenic is mostly found. This substance is introduced because of its antifermentative properties. The gastrointestinal disturbances provoked by it are of frequent occurrence in Russia, where preserved fish is extensively used.

Finally, foods may contain other metals given off by cooking utensils and vessels made of pewter and nickel, which, however, do not seem to be dangerous.

Among the toxic substances found in foods it is well to mention the aniline colours, which too often contain arsenic and which are used to colour wines, bonbons, and sirups.

Of all poisonous substances added to foods, one of the most extensively used is *salicylic acid*. This acid, employed to prevent putrefaction, is well supported by normal persons; but it often induces grave manifestations in those whose kidneys are more or less markedly altered, and therefore unequal to the task of eliminating it by the urine.

To sum up, three substances claim our attention—namely, arsenic, salicylic acid, and, above all, the lead salts.

Poisoning may also be occasioned by the use of nonedible *vegetables* or *animals*. We hardly need refer to the frequency of disturbances caused every year by poisonous mushrooms or toadstools, the action of which is due to three poisons—namely, choline, muscarine, and phalline. Accidents have sometimes been observed as the result of the use of sprouting potatoes sold as new; in fact, upon the skins there is found a violent poison—namely, solanine.

It is mainly in hot countries that *venomous animals* are encountered. In our latitudes the accidents are produced by the eggs of certain fish, such as herring, pike, molluscs, oysters, and sometimes certain crustacea.

Fish eggs provoke choleriform phenomena—that is, vomiting and diarrhœa accompanied by general prostration; afterward cutaneous manifestations appear, such as erythema and urticaria. Recovery is the rule.

The toxicity of fish is due, it seems, to their having lived in water containing putrefying matters, notably near coral reefs. A similar explanation may be given for the action of molluscs. Poisonous oysters are those that have lived in unwholesome surroundings—for example, near the outlets of sewers. Shellfish may be particularly dangerous. It was once asserted that they became toxic when they lived upon the sides of ships sheathed with copper.

Even when healthy, shellfish are not good food. The inhabitants of Tierra del Fuego, who consume as much as 5 to 15 kilogrammes a day, are affected with a special hepatic cirrhosis attributed to this form of diet.

Under certain circumstances the flesh of animals may become toxic—for example, when they are overworked. This is due either to the fact that overwork provokes the development of noxious substances or because it permits the intestinal microbes to pass into the tissues. Thus it is with good reason that animals destined for food are allowed to rest for at least twenty-four hours before they are slaughtered.

Accidents have been provoked by the use of the flesh of animals receiving toxic substances. This is not always the case, however, as savages consume the beasts killed by poisoned arrows. Nevertheless, morbid manifestations may appear when use is made of the flesh of mammalia which have received high doses of arsenic for therapeutic purposes.

In the course of diseases, and notably of infections, toxic substances may be produced which are again met with in the tissues or the secretions. The flesh and milk of animals dead from indigestion, dropsical cachexia, various infections, and particularly puerperal fever, should be absolutely rejected.

Aliments of vegetable origin may produce disturbances, either because they come from diseased plants or because they have been invaded by various parasites.

Numerous epidemics, which have been described as *ergotism, feu Saint-Antoine*, raphania, are known to be provoked by ergot—*Claviceps purpurea*. The disturbances are due to various substances, of which one, sphacelic acid, causes gangrene of the extremities, and another, cornutine, produces convulsions. The disease in man assumes two different types, which may either have a gangrenous or a convulsive form.

Among the alterations of cereals, it is sufficient to mention nigella

and the wheat rot, the mixture of flour and *Lolium temulentum* (bearded darnel), and the copper green of Indian corn, which plays an important part in the etiology of pellagra.

Volatile Poisons. Poisons of the Air.—Apart from alimentary poisons, numerous others are daily met with. Volatile poisons are found in the atmosphere. *Confined air,* vitiated by the respiration of several individuals, soon becomes toxic and produces indisposition and giddiness. When a great number of persons are inclosed in a small room, death may supervene. It is not merely a question of diminution of oxygen or accumulation of carbonic-acid gas, but one in which the toxic substances are of organic origin and impart to the air a well-known nauseating odour.

Air may be polluted by *products of combustion*—for example, by carbonic-acid gas, which is not very dangerous, and especially by carbonic oxide. Poisoning by the latter gas occurs quite frequently when movable stoves with slow combustion are employed. In this way as high as 16 per cent of carbonic oxide is produced (Moissan). When there is little or no draught, the slightest puff of wind drives the deleterious gas into the room or even into the adjoining apartments. This is also a source of poisoning, manifesting itself by constant headache, loss of memory, and anæmia, and one which, in certain cases, may assume an acute course, resulting in death.

The combustion of illuminants also produces carbonic oxide. The oil lamp, however, gives off almost exclusively carbonic-acid gas.

Illuminating gas is very toxic, because it contains from 7 to 20 per cent of carbonic oxide. In Paris 150,000,000 cubic metres of it are manufactured. Ten per cent, say 15,000,000 cubic metres, are lost in consequence of defects and infiltrate the soil. On approaching a trench opened in the street we smell the strong odour of gas. It is no wonder, therefore, that the atmosphere of Paris contains 1 per 10,000 of carbonic oxide. A much greater proportion seems to exist in apartments which, by virtue of their high temperature, draw the gas distributed to the soil.

The air of apartments may also be polluted by substances emanating from paintings and tapestry. This was formerly a frequent occurrence when arsenical greens were extensively used.

Finally, as if all these causes of intoxication were not enough, the majority of men poison themselves by the daily use of tobacco. Every year 2,000,000,000 kilogrammes of this plant are consumed. In France the consumption exceeds 30,000,000 kilogrammes. In the smoking of tobacco carbonic acid, carbonic oxide, sulphuretted hydrogen, hydrocyanic acid, traces of nicotine, and especially pyridic bases are inhaled. The last-mentioned substances are the most dangerous

of all; they are particularly abundant in a slow and incomplete combustion—as, for example, in pipe smoking.

Generally, the habit is quickly formed, but the abuse of tobacco gives rise to many disturbances—namely, diminution of memory, especially for proper names, dyspepsia, palpitation, spells of angina pectoris, which, though generally harmless, sometimes kill, as happened in a case reported by Dr. Letulle.

While those who smoke are poisoned, chewers are far worse affected, because they ingest the various toxic substances contained in tobacco, notably nicotine. In those who are not accustomed to its use disturbances rapidly appear. Some persons have been seen to succumb from the effects of chewing half a cigar.

In Oriental countries the smoking of opium replaces that of tobacco. In China they begin to smoke at about the age of eighteen; it is not, however, in their own homes that they give themselves up to this occupation; it is in more or less luxurious dens where they assemble or remain isolated.

They very quickly become accustomed to the poison, and soon reach daily doses of from 5 to 6 grammes of the extract. The habit does not seem to be very pernicious; it is much less so than the practice of eating opium. Eaters of opium and of theriaca, especially numerous in Turkey and Persia, present a premature decrepitude.

In European countries opium is nowadays causing great ravages under the form of morphine injections. It is on the occasion of a pain, a neuralgia, or an insomnia that the first injection is resorted to; then the habit is formed, and very considerable doses are reached—0.5 to 1 gramme, and even 4 to 5 grammes daily.

Morphinomania is prevalent mainly among the higher classes. It is of very frequent occurrence in persons who can easily procure morphine. In the statistics of Dr. Pichon, comprising 66 subjects, there were 17 physicians, 7 students of medicine, 5 druggists, and 3 students of pharmacy; out of 56 women, 12 were married to physicians.

Other poisons may be employed for the agreeable sensations they produce. Such are ether, cocaine, chloral, and especially hasheesh, prepared with the leaves of *Cannabis indica*, which is used by 200,000,000 to 300,000,000 people in Africa, India, and Turkey.

In Oriental Asia an inebriating beverage is prepared from a poisonous mushroom—the false orange.

Poisonings due to Occupation.—In approaching the study of poisonings due to occupation we again meet the poison with which we have become familiar—namely, *lead*. Disorders may be produced during the extraction of the mineral from the earth. The miners die young, their average age not exceeding forty-two, and their mortality

amounts to 18 per cent a year. In France the disorders are mostly observed in workers in white lead and in painters. A few years ago the workmen in the factory at Clichy (France) entered the hospital on an average of four times a year. Owing to the introduction of better sanitary conditions, accidents are now of much less frequent occurrence. They occur mainly among painters, who are first attacked with lead colic and later with arteriosclerosis, paralysis, interstitial nephritis, and gout. Arteriosclerosis is a pernicious manifestation, and when the arteries of a young man are found to be very hard, saturnine poisoning can almost certainly be diagnosticated.

Mercury, like lead, also produces grave disturbances in workmen employed in its extraction. The miners of Almaden, in Idria, are affected with a special gingivitis resulting in shedding of the teeth.

There has been a good deal of loud talk of late, and with just reason, in reference to the disturbances caused by *phosphorus*. The workmen in match factories are affected with an extremely serious necrosis located in their lower maxillary bones. This lesion is comparatively rare to-day, owing to a better equipment of the factories, and especially to the use of the harmless red phosphorus, which is gradually tending to replace the white phosphorus.

The combustion of *coal* may produce two kinds of intoxication: one due to arsenic, the other to carbonic oxide. Coal always contains some arsenic, which passes into the smoke, and, in the neighbourhood of factories, especially of furnaces, is deposited on the soil and vegetables, and thus may produce poisoning in man and animals.

Carbonic oxide is much more widely diffused. It intervenes very often in the habitual conditions of life. Cooks and laundresses, who breathe it constantly, are affected with anæmia and disturbances of memory. There are records of several cases of persons having been killed as the result of lying down near a furnace.

There are other deleterious gases to be pointed out, such as nitrous vapours, chlorine disengaged in the bleaching of paper, and gases emanating from animal matters undergoing putrefaction. This is what is called *mephitism*.

Accidents produced by these emanations were formerly very frequent among workers in sewers; but to-day the ventilation of sewers is so perfect that the danger has disappeared. The same is true of cesspools, where accidents are no longer observed except in time of repairs. In detaching the crusts covering the walls of sewers and cesspools, hydrosulphate of ammonia is disengaged, the inhalation of which causes rapidly fatal accidents. We may also mention the volatile products emanating from putrid organic matters in tanneries, catgut and glue factories, and the like.

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Poisoning by Drugs.—Another group of toxic causes comprises the medicinal substances. To say nothing of errors of dosage, there are poisonings caused by the impurities of certain products. Glycerine may contain arsenic; strontium salts are not always free from baryta. It should be remembered that tinctures and extracts, even when well prepared, are very unreliable, as they contain variable proportions of the active principles. Hence, the tendency is to substitute for them alkaloids and glucosides, which are quite definite from a chemical point of view; they do not, however, always manifest the same action as the more complex and less purified products.

Accidents are often brought about by the use of medicine for too long a period. It was once believed that mercury did not produce its effects until it gave rise to salivation. At the present day accidents of this nature are no longer observed; but toxic manifestations are sometimes produced by injections of bichloride of mercury and the long-continued administration of digitalis.

It may be well to here remark that the stomach does not easily bear most of the medicines introduced into it. In many cases chronic gastritis is simply the result of abuse of therapeutic substances, and a good many of the troubles due to alcohol are traceable to the use of so-called tonic or rejuvenant wines.

Anæsthetics have caused a certain number of deaths. Nitrous oxide seems to be harmless when used for very short operations and inhaled only a few seconds. Out of 30,000 cases reported in America there is not a single death. On the contrary, according to Morgan's statistics, chloroform has produced 34 deaths out of 100,000 cases, and ether only 4 for the same figure. In America these results have led to the substitution of ether for chloroform in surgical anæsthesia; in France, also, a similar tendency is now observed.

Criminal Poisoning; Suicide; Accidents.—Poisons are frequently employed for criminal or suicidal purposes. Arsenic was formerly the one most frequently made use of. It was the basis of the Borgia poison, and was employed by the Marquise of Brinvilliers. Nowadays the progress of chemistry leads criminals to avoid the use of mineral poisons, since they are easily detected. The vegetable alkaloids are preferred, because they induce no lesions and are with great difficulty distinguished from cadaveric ptomaines. For this reason experts are often unable to arrive at a positive conclusion.

Suicide is often committed by means of alkaloids or cyanide of potassium. In France the fumes of coal—that is, carbonic oxide—are resorted to. As a matter of fact, 185 cases of asphyxia have been reported as against 52 poisonings. In other countries the proportions are quite different. In Italy, for example, there were 44 cases of

asphyxia and 132 poisonings; in Prussia, 11 to 20; in England, out of 225 cases of poisoning there was not a single example of carbonic asphyxia.

Poisons have also been utilized for judicial purposes. In Greece, the condemned persons were made to drink hemlock. The countries that we call barbarous had poisons of trial. For example, in Madagascar, on certain days the extract of Calabar bean was administered to 500 to 600 persons. Those who did not die were declared innocent. The same method was used to decide legal questions. The system, however, soon became modified: each adversary was represented by a dog; the two animals drank the poison, and the owner of the one that died was pronounced guilty and condemned.

Venoms.—Venomous animals are those possessing venom glands, the contents of which can be exuded. These should not be confounded with poisonous animals. The latter contain toxic substances in their blood and tissues. We have spoken of them in treating of alimentary intoxications.

Among the venomous animals the most dangerous are represented by the *ophidia*. All snakes are possessed of a venom gland; but in some of them, as in the case of *couleuvres*, the gland being deprived of an excretory duct, the poison can not be poured out. The Montpellier adder, whose gland opens at the bottom of the buccal cavity, is harmless for man and for animals of great size; it can kill only small animals, which it seizes by one of the limbs.

The venomous species of France are three in number: the *Vipera aspis,* which must not be confounded with the asp of Egypt, the *Vipera ammodytes,* and the *Pelias berus.* Our (France) indigenous vipers are more dangerous in the south than in the north, and on the left than on the right bank of the river Loire. Their bite may occasion the death of an adult, and more readily that of a child; but even when the bite is healed, it is in many cases followed by persistent neuralgia, recurring sometimes at certain seasons.

Although serpents are not very dangerous in our (France) latitudes, they constitute a veritable evil in hot countries. In India 20,000 persons die each year from their bites.

The effects provoked by serpents are divided into local and general disturbances. Locally, œdema appears, especially marked when the venom is not very active; it is also observed as a result of the bites of our vipers. Œdema has developed sufficiently in certain regions of the body to mechanically cause a fatal termination.

The general disturbances are characterized either by progressive asphyxia (proteroglyphes) or by convulsive phenomena (solenoglyphes).

After much discussion, it is acknowledged that snake poison consists essentially of proteid matters and albumoses. To combat its effects, the first thing to do is to oppose its absorption. Tying the bitten limb and suction of the wound are well-known procedures. Next, we resort to cauterization and hypodermic injection of substances that neutralize the venom—for example, potassium permanganate, gold chloride, and, above all, calcium and sodium hypochloride. Lastly, it has been recognised of late that it is possible to accustom animals to progressively increasing doses of venom; their blood acquires curative properties and their serum has been used with success. The names of Phisalix, Bertrand, and Calmette are connected with this discovery.

The other animals capable of producing venom are less important. In European countries there are the *toad, triton,* and, above all, the *salamander.* Among fish there are *trachinidæ* (weever, stingfish), which secrete themselves in the sand, and the bite of which may produce in bathers phlegmons and gangrene, often of very grave character.

Venomous insects are very disagreeable, but generally not very dangerous. The bites of gnats, bedbugs, fleas, and ants are without gravity. It is estimated, however, that six to eight hornets can kill a man. In some cases a wasp has bitten in a region where the consequent swelling has caused death—for example, at the base of the tongue or in the pharynx.

The active principle of the venom of the bee and hornet consists of formic acid united to a hydrocarbon—undecane, the formula of which is $C_{11}H_{24}$.

Finally, we may mention the *scorpion* of the south of France, the bite of which is of little gravity.

Modes of Penetration of Poisons.—Poisons can penetrate our organism in several ways. They enter mostly by the digestive canal, which is provided with certain means of protection. The disagreeable, acrid, or burning taste of certain substances causes one to expectorate immediately, and at the same time provokes a salivary secretion, which cleanses the buccal cavity. If some of the poisonous substance has been swallowed, antagonism is manifested in the stomach: First, by an abundant secretion, which hinders absorption, dilutes the poison, and neutralizes certain principles; next, by rejection through vomiting. Finally, when the poison reaches the intestine, similar phenomena are produced—namely, an increase of secretion and evacuating diarrhœa. It may be remarked, however, that the diarrhœa which supervenes in cases of poisoning is mainly in connection with the secondary elimination through the mucous membrane of the intestine.

The poison may find in the digestive canal conditions favourable

for its harmful action. For example, fatty matters dissolve phosphorus and hasten its absorption; the hydrochloric acid of the stomach transforms calomel into corrosive sublimate, and the insoluble carbonates into soluble chlorides; it also decomposes potassium cyanide and thus gives rise to hydrocyanic acid. Hence it is that the action of the substance last mentioned is less marked when the stomach is empty than during digestion.

If the poison be a gas, other protective phenomena intervene. The odour, the pricking of the mucous membranes, the irritation that provokes lachrymation, sneezing, or coughing, warn us of danger. These reactions are not constant, however, and absorption does take place. Gases penetrate very easily through the lungs; even liquids introduced by this route can be absorbed, provided they are introduced very slowly.

Volatile substances can also penetrate through the skin. For example, mercury, iodine, turpentine, and methyl salicylate are readily absorbed in this way. Certain solids, especially when they are incorporated with fats, can also pass through the integument.

Absorption by the *urinary apparatus* has been a subject of much discussion. The prevailing opinion is that the bladder does not absorb; contrary results are due to the fact that too strong solutions have been injected, which alter the epithelial lining and abolish its protective function. Another cause of error capable of vitiating experimental results is that the posterior urethra absorbs very well; a drop flowing from the bladder can occasion poisoning. Very little, if any, absorption can take place in the ureters, but it doubtless occurs in the calices. In women, the vagina, and still more the uterus, may serve as routes of penetration for poisons; and in numerous cases accidents have occurred as the result of the too prolonged or continued use of corrosive sublimate.

The subcutaneous route is daily used in the therapeutic introduction of medicines. Absorption is the slower the thicker the subcutaneous fatty tissue is, and it varies also according to regions. The different parts of the body may be classified as follows: First, the temples and cheeks; second, the epigastric region, the inner surfaces of the thorax, the external surfaces of the arms and thighs, the foot, and, last of all, the back. From a practical standpoint these results are evidently very important. Absorption can also take place in exposed *mucous membranes*, such as the conjunctiva, and in *serous membranes*, such as the pleura or the peritoneum.

Among the conditions antagonizing or favouring absorption we must note certain modifications of a physical order. A decrease of pressure upon the integuments retards absorption. This is what is realized by suction or by dry cupping. If, however, pressure in the

abdominal cavity be increased, the passage of colloids, like the albumins, is hindered, while that of crystalloids is enhanced. This result, which has greatly surprised certain authorities, is altogether in accordance with physical laws. The same effects are observed when a liquid is made to pass through a porcelain filter: the increased pressure hastens the passage of the water and of the salts dissolved in it, but causes a dissociation of albumins, which are not carried off by the current but retained on the filter.

Since the time of Magendie it is admitted that bloodletting favours absorption, while intravenous injections of salt water delay the passage of substances by increasing the mass of blood. These results are exact, although far more complex than was believed. The effect of injections of water is notably to modify the reactional power of the nervous centres and the secretory rôle of the kidneys. This is what renders the problem so difficult and the interpretations so very delicate.

The absorption of toxic substances is determined chiefly by the venous system. Magendie has perfectly demonstrated this by an experiment which has become classical. He divided the thigh of a dog and united the two ends of the severed artery and vein by glass tubes; he introduced poison into the paw thus connected with the rest of the body, and toxic manifestations were produced. The poison could not have penetrated except by the blood vessels, since the lymphatics no longer existed.

Transformation, Elimination, and Accumulation of Poisons.—After reaching the blood, poisons act differently, according to the manner of entrance. If they enter through the digestive tract, they pass into the mesenteric and portal veins and arrive first at the liver. Placed as a barrier in the path of all substances coming from the gastro-intestinal apparatus, the liver exerts on them a selective action; it allows some to pass on, retains others, and, after having stored them up for some time, permits them to gradually pass again in harmless amounts; it eliminates some of them through the bile, and, finally, it submits many others to chemical transformations, depriving them of their toxicity. These modifications are especially brought to bear upon the alkaloids, so that a poison loses about half of its toxicity in passing through the hepatic gland. Here, then, is an important protective rôle to which we shall more than once refer.

When it has passed through the liver, or when it has penetrated directly through the skin or subcutaneous tissue, the poison reaches the vena cava, passes through the heart, and arrives at the lungs. Here is another protecting organ. It acts upon certain alkaloids, notably upon strychnine; but it especially eliminates volatile substances. Sulphuretted hydrogen, for instance, which is very toxic when inhaled,

can be introduced by the stomach or the rectum without inconvenience; it is exhaled by the air as fast as it penetrates. Phosphorus is also eliminated by the lungs, and imparts to the expired air the property of luminosity in the dark. The other gaseous substances follow the same route, since it is possible to notice them by the characteristic odour of the breath.

After passing the pulmonary barrier, poisons arrive at the left heart, and from there pass on through the aorta to be distributed to the different parts of the organism. They reach the nervous system, where they produce the principal disturbances due to their action. Part of the poison, however, passes through certain protective organs, such as the sanguineous vascular glands; another part encounters organs which throw it out. Poisons thus pass into secretions—sweat, milk, tears, and especially the urine.

The .kidney, in fact, represents the principal route of elimination for the majority of toxic substances. Finally, a certain amount of poison may return to the stomach and intestine by the mesenteric arteries and cœliac axis, and be eliminated by the glands of the digestive canal. Morphine, for example, passes into the gastric secretion; therefore, in cases of poisoning by this alkaloid, it is well to wash out the stomach even when the poison is introduced by the hypodermic route. The poisons passing out by way of the intestines may produce diarrhœa and sometimes alter the mucous membrane, which is then placed at the mercy of the numerous intestinal microbes. Thus a gangrenous enteritis results under the influence of corrosive sublimate. It is a lesion induced by the elimination of mercury and determined by the intestinal bacteria.

Certain conditions intervene to favour or hinder the elimination of poisons. In children, the kidneys work with extraordinary energy, and this is why poisons which can be eliminated by the urine are so well borne by children. The same doses of salicylate of sodium given to an adult can be given a child of six years.

In the old, on the contrary, elimination is slow. Much caution, therefore, is to be exercised in the administration of active medicines to the aged.

Finally, elimination is modified during the course of various organic affections—for example, in nephritis, the urinary function being insufficient, active substances easily provoke disturbances.

Poisons accumulate mainly in two parts of the economy—namely, in the liver and the osseous system. The analyses of toxicologists teach us that arsenic, lead, and mercury are able thus to remain for years. Hence the possibility of disturbances breaking out long after the use of a poison has been suspended. Kussmaul reports that two

persons developed salivation on the occasion of a sulphur treatment four and twelve months respectively after having ceased the employment of mercury.

The possibility of these accumulations should not be lost sight of in practising therapeutics; doses perfectly well borne at first may produce disturbances at the end of a few days; such is the case with digitalis.

Toxic Equivalents: their Variations.—The considerations we have presented already explain that a toxic substance does not always produce the same phenomena in the same doses.

In the first place, there are variations dependent upon the species. Take nicotine, for example. The fatal dose of this alkaloid, reduced to the proportion of 1 kilogramme of animal, is represented by the following figures: 35 milligrammes for the frog, 12 milligrammes for the guinea pig, 7 milligrammes for the rabbit, 5 milligrammes for the dog, and 0.5 milligramme for man. As a rule, the higher the being is in the animal scale, the keener is its susceptibility.

In the next place, variations according to *races* are to be taken into account. Darwin furnishes numerous examples: the white sheep and hog are more sensitive to certain poisons than those of dark colour. In man, morphine calms a European, while it excites and drives a Malay to homicide.

Fatal doses vary also according to *age*: more poison is required, weight for weight, for killing a child than an adult, and especially an old man. The influence of *sex* is quite evident in the following figures, given by Preyer: To kill a male guinea pig 8 milligrammes of curare are required; for a female, 13 milligrammes; and in the case of a pregnant female, as much as 17 milligrammes.

A condition of another order is represented by the *temperature* of the body. Thermal elevation favours the action of poisons. The surrounding temperature may have variable effects; it renders the organism more sensitive to convulsive poisons, but facilitates the elimination of certain substances. If we give the same dose of chloral to three guinea pigs, we see the one left in the open air die in four hours; the second, wrapped in cotton, will survive after a sleep of twenty-four hours; the third, placed in an oven, will recover in seven hours. By cooling certain animals, and by heating others, we can further vary the fatal doses.

The state of *fasting* or *digestion* should also be taken into consideration, and likewise the integrity or lesions of various organs, particularly those that are concerned in the transformation and elimination of toxic substances. Finally, there exist particular *idiosyncrasies,* resulting from a series of inappreciable causes which impart

to beings a resistance and predisposition impossible to determine in advance.

It may be understood how difficult it is to exactly establish the fatal dose of a substance. A great many attempts have, however, been made in this direction, and have already led to results of much interest. By operating on animals and injecting poison into the veins, it has been possible to determine the deadly dose. Dr. Bouchard proposes to designate the quantity of poison capable of killing a kilogramme of animal by intravenous injection as the *toxic equivalent.* It is evident that the toxic equivalent is applicable only to the species on which the operation has been made, and that it would not be exact to transfer the results from the animal to man. We can only obtain interesting indications.

If figures determined in experimenting upon animals are fairly concordant, effects observed in man are far more variable. Thus, in certain cases, 0.3 gramme of extract of opium has proved fatal; in other cases, 1.5 gramme has been endured. The results are the same for morphine: 0.4 may kill and 2 grammes may not cause death; 1 centigramme of atropine sulphate generally represents a deadly dose, whereas some persons have tolerated 25 or 30 centigrammes; and with cocaine, 4 centigrammes have killed in one case; 1.25 gramme has not done so in another.

Habit.—Finally, it should not be forgotten that one soon becomes accustomed to certain poisons. Tobacco, alcohol, and morphine, which first arouse painful reactions, are very well borne after some time and even seem to become indispensable to life. A familiar illustration is afforded by the history of the amœba, which can gradually be habituated to water containing 2 per cent of sea salt; it becomes so accustomed to the new conditions that it perishes when again brought back into ordinary water. Under the influence of poisons frequently introduced, a modification of cellular nutrition is effected, with consequent humoral changes: the humours become antitoxic in nature—i. e., they acquire the property of neutralizing the noxious effects of substances to which they have become habituated. Here a new field is opened to therapeutics.

Anatomical Lesions of Toxic Origin.—In producing functional troubles, poisons gradually modify the structure of cells—i. e., give rise to anatomical lesions in them. They may produce local manifestations, pus, or sloughing. In other cases they induce alterations in organs or tissues. Among these, some are common manifestations: hemorrhages, muscular ruptures provoked by contractures and convulsions, emphysema due to respiratory disorder, and subpleural or subpericardial ecchymoses induced by asphyxia. Others are to be con-

nected directly with the action of poisons. If it is true that functional disturbance always precedes the anatomical lesion, it is easy to understand that the poison will exert its effects first upon the most clearly differentiated elements—i. e., upon those that act effectively. The lesions of connective tissue will be but secondary. In the kidney, for instance, it is always the epithelium that is first attacked; in the liver, the hepatic or biliary cells; in the spinal cord, the great nerve cells. If among these affected cells some should succumb, the defect thus produced will be supplied by connective tissue. Thus what is called sclerosis is developed. The function of the connective tissue not being deranged, we can not conceive it to be the seat of primary lesion. Its development is a phenomenon of reparation, comparable to a cicatrix.

Finally, in cases of chronic intoxications, nutritive modifications are produced, sometimes finding expression in emaciation (morphino-mania), sometimes in obesity (alcoholism), and in still other cases in some curious phenomenon, as uricæmia and gout (saturnine).

The various disturbances provoked by toxic agents may be transmitted to descendants. It is thus that beings come into the world with organic taints and nutritive vices; and, as the morbid impression will have acted on young and easily impressionable cells, the disorders acquired by parents will often be found exaggerated in their offspring.

CHAPTER V

ANIMATE AGENTS

Parasites and infectious agents—Definition of infectious diseases—History—Spontaneous generation, fermentations—The work of Spallanzani, Davaine, Pasteur—Division and cultivation of infectious agents—Bacteria: their classification, their variability.

THE animate agents are usually divided into two groups—parasites and infectious agents.

Some writers have thought that natural history could be taken as a basis for this distinction. According to them, infectious diseases are those caused by bacteria. This conception, however, seems scarcely admissible, for the group of infectious diseases was created before the discovery of bacteria, and hence was of necessity established upon the data of clinical observation. It is only by comparing the morbid processes, by taking into account the conditions of their development, the manifestations they have presented, and the evolution they have followed, that it has been possible to draw closer together certain diseases and group them. The bases of the classification, therefore, have been symptomatic. It was and still is the only possible classification. Since the apparent signs are to be traced to hidden occurrences, it has been and it always will be necessary to start from what we see—namely, from clinical manifestations—and it is only by deduction that the cause of observed disorders can be affirmed.

When the animate nature of pathogenic agents was discovered, it was desired to establish a relation between infectious diseases, as they have been defined, and the microbes which were disclosed. But such relations do not exist. Malarial fever, which everybody classes among infections, is due not to a bacterium, but a sporozoid. The type of infectious diseases, tuberculosis, seems to depend upon a relatively high fungus or a streptothrix akin to actinomyces. Yet no one would dare maintain that malaria and tuberculosis must be thrown out of the class of infectious diseases.

We therefore conclude that infectious agents may belong to classes other than bacteria, and that there is no constant relationship between their taxonomic position and their action on living beings.

What, then, is the difference between parasitic and infectious agents?

A chief distinction is furnished by the way in which the two kinds of agents act toward the individual upon whom they live. The parasite spares his host; it does him the least harm possible; it draws exactly what it needs for its own subsistence; it understands that it is to its own interest to preserve for the longest possible time the individual upon whom it lives.

The infectious agent does not take all these precautions. It acts with brutality: develops rapidly, tends to invade the entire organism, disturbs its functions, excites very intense reactions. It engages in a terrible struggle, the issue of which varies according to a number of secondary circumstances.

The parasite is satisfied with the corner where it vegetates; it grows slowly, expands very little, and it hardly, if ever, invades the economy; and if, at a certain moment, it causes death, it is, as it were, accidentally, unwittingly. Example: The intestinal worm when it makes its way into the air passages. In this way the parasite, satisfied with little, is easily supported; it does not give rise to violent reactions; often it remains even unnoticed. It may, however, grow, and when its volume becomes considerable, it may produce various disturbances. Such is the case with a hydatid. But the phenomena provoked here are due to compression; they are of a mechanical order. On the contrary, infectious agents act chiefly by the fermentations which they produce and by the toxic substances which they engender. There precisely lies the chief difference. No doubt, as in all distinctions, this is not an absolute one. Parasites also produce toxic substances; some are found in the liquid of hydatids. It is always a question of more or of less. But, with parasites, intoxication is reduced to a minimum; with infectious agents, it becomes predominant and explains all the reactionary phenomena. Infectious diseases may therefore be defined, *" Diseases developed under the influence of toxines produced by certain parasitic agents."*

Infection, then, is nothing else than a chapter of intoxication.

History.—Three terms characterize all infections: an animate agent, a fermentation, an intoxication. These three terms are encountered in the writings of the most ancient observers.

From Varro and Columelle to Linnæus, only beings relatively high in organization were considered capable of producing infectious diseases. This gross parasitism which attributed a pathogenic action to

worms, insects, or arachnidæ, attained its height with the theories of Raspail on sarcoptogenesis.

With the idea of comparing viruses to poisons evolved simultaneously, *typhic* or *paludal intoxication* was spoken of, though without attaching a very precise meaning to these expressions. There was only a tendency to consider certain *miasms* as volatile poisons.

Finally, since Rhazes, who likened smallpox to the fermenting must of grapes, many physicians—Hoffman, Braconnot, Bouillaud—compared the infectious to the fermentative process. It was the comparison of an unknown phenomenon with another which was no better known. Up to recent years the nature of these two great processes was completely obscured, and whenever a happy chance permitted the discovery of a living being in a diseased organism, in putrescent matter, or in a fermenting liquid, it was simply supposed to be a case of spontaneous generation.

The first author who revolted against the nefarious yoke of the belief in spontaneous generation, which had dominated since Aristotle, was a naturalist of the seventeenth century, F. Redi. The experiment which he realized, no matter how childish it may seem to-day, possessed at that epoch vast importance. Redi established the fact that the larvæ of flies were not born spontaneously through putrefaction of meat. By means of a gauze, he prevented the insects from depositing their eggs, and henceforth the larvæ did not develop.

A few years later, in 1678, van Leeuwenhoek, examining vegetable infusions, observed the presence of microscopic beings, which Wrisberg, in order to recall their origin, named infusoria. Van Leeuwenhoek understood that these beings were not born by the decomposition of matters, but that they proceeded from pre-existing germs, spread in the atmosphere. This very same idea was again taken up in the following century and developed, in a series of admirable studies, by Spallanzani. Stimulated by numerous attacks directed against him by Needham, Spallanzani multiplied his researches and established the fact that there is no fermentation when the liquids are protected from air. This great discovery was confirmed by Schultze and by Schwann. Finally, in 1837, Cagniard-Latour showed that during alcoholic fermentation yeast increases and multiplies absolutely like a vegetable.

Yet, despite the observations made by van Leeuwenhoek, Spallanzani, and Cagniard-Latour, the question of fermentations remained very obscure. The progress of discoveries was arrested by the belief in spontaneous generation, which still persisted, and by the false theories that had been accepted upon Liebig's authority. The fermentative process was attributed to a particular condition of matter, exercising some kind of a catalytic action.

It was then that Pasteur undertook the study of the problem. Completing the researches of Spallanzani, he demonstrated that innumerable germs are hovering in the atmosphere, and that, falling into certain liquids, if they there find the conditions favourable for their development, they determine fermentation. Pasteur then conceived the brilliant idea of isolating and cultivating these germs, and he thus succeeded in describing successively, in 1857, the lactic ferment; in 1860, the alcoholic ferment; in 1861, the butyric ferment. This last ferment differed from all beings known up to that time by the fact that it lived without oxygen; it was the first example of anaërobiosis.

These works aroused numerous protestations on the part of chemists. Physicians took no interest in them, as they failed to see the applications which they could make of them to medicine. Only one man saw clearly: that was Davaine.

In 1850 Davaine discovered the first pathogenic microbe that had ever been seen. Examining the blood of sheep dead from anthrax, he discovered small motionless and refractive rods, of which he did not suspect either the nature or the meaning, and to which he only attributed a diagnostic value. These same elements were again found in 1855 by Pollender, and in 1857 by Brauell, who observed them in the blood drawn from the living animal. In 1860 Delafond, by a spark of genius, determined that these rods were vegetables. He made some attempts to cultivate them in the blood, saw the rods grow in the form of filaments, and it even occurred to him to look for spores, which he failed, however, to bring to light.

The following year appeared Pasteur's work on butyric ferment. Its perusal threw light on Davaine's mind and brought him back to the study of the vegetable which he had seen in the blood of animals suffering with anthrax. He learned that infectious diseases were produced by microbes, just as are fermentations. He undertook a series of researches, the results of which he published in 1863. This brought down upon him an avalanche of criticism and gave occasion to contradictory experiments. Signol, Leplat and Jaillard, Sanson and Bouley, to cite only the principals, endeavoured to prove that the bacteridia of Davaine are not found exclusively in the blood of animals affected with anthrax; that they had no specific value, and that putrid blood swarmed with similar microbes, equally capable of killing animals.

Davaine had no trouble in refuting these objections. He showed that his adversaries were mistaken; that they confounded anthrax and septicæmia, and that the microbes found in putrid blood are the agents of a special process of which he made a remarkable study.

We can not help admiring Davaine when we think of the work achieved by him under the most unfavourable conditions! A simple practising physician, Davaine could only work in his small property in Garches or in caves placed at his disposal by a friend. It was under these defective and discouraging conditions that Davaine took up and solved the principal problems relating to infectious diseases. Is it not really a great pity that such discoveries were not appreciated enough to give their author an official position or to create for him a laboratory?

However, the impulse was given. On all sides the study of the pathogenic problem was taken up. It was Villemin who first established, in 1866, the inoculability of tuberculosis. In 1867, Chauveau demonstrated that in virulent liquids the active part does not pass through a porcelain filter. In 1872, Coze and Feltz published a series of researches on infections, and had the merit of perceiving the streptococcus of puerperal fever. Simultaneously, in Germany, Cohn and Nägeli isolated a series of saprophytic microbes and indicated the means of cultivating them. In 1875, Koch entered upon the scene with the discovery of the anthrax spores.

Prepared as he was by his researches on fermentations, Pasteur undertook the study of diseases. He first took up the lower beings and published researches on the diseases of silkworms highly instructive for human pathology, but to which the medical world paid no attention. Passing then to the diseases of mammalia, Pasteur undertook the study of anthrax. In 1877, he supported with his authority Davaine's researches, and made known the means for the cultivation of pathogenic bacteria. He thus created the fundamental methods of bacteriology, a field which Koch was soon to perfect by the use of solid media. These procedures, so simple and so sure, permitted the isolation successively of a whole series of pathogenic agents, and rendered it possible to obtain them in pure cultures and to reproduce in animals the diseases observed in man.

The first discoveries gave rise to vigorous opposition; but, little by little, the adversaries were silenced, and were forced to yield to the accumulating works and to bow before the achieved results. In less than twenty years this great scientific revolution was accomplished, with Davaine as its pioneer and Pasteur as its artisan.

Division of Infectious Agents.—The first bacteriological discoveries led to a conception which for a moment nearly impeded all progress. By an induction easy to understand, it was believed that every disease was caused by a well-defined, special microbe. We know to-day that this is not so, and we can in this regard formulate the two following laws, which govern the whole history of infectious diseases:

The same microbe may produce diseases the clinical manifestations of which are absolutely different.

A disease, clinically well defined, may be produced by different microbes.

Let us take, for example, a widespread microbe, streptococcus: it produces pus, erysipelas, septicæmia, pyæmia, lymphangitis, pseudo-membranes, gangrene, visceral inflammations, etc.

Reciprocally, a well-defined affection, like broncho-pneumonia, may be due to most varied microbes, as streptococcus, staphylococcus, pneumococcus, pneumobacillus, coli bacillus, etc.

Therefore there is no necessary and constant relation between diseases as they are clinically determined and pathogenic agents as they are made known by bacteriology.

Such results must not surprise us; they do not differ from those observed in studying other pathogenic agents, notably the poisons. Alcohol, for instance, produces inebriation, delirium tremens, hepatic cirrhosis, pachymeningitis, peripheral neuritis, etc. It is always the same poison, except that it acts under different conditions.

On the other hand, the manifestations just mentioned may be referable to most diverse toxines; peripheral neuritis, for instance, may be engendered by lead as well as by alcohol.

We are thus led to admit that, from a medical point of view, infectious agents may be divided into two groups: *specific* and *nonspecific agents.*

The former are those which determine diseases always similar to themselves, or at least diseases which present common characteristics enough to enable us to relate to each other the various clinical forms; such is the case with typhoid fever, anthrax, glanders, and tuberculosis.

The second group, numerically the more important, comprises agents apt to produce the most dissimilar clinical types. They are, as Peter said, all-round microbes (*microbes à bout faire*). Let us take, for instance, *Staphylococcus aureus.* According to its localization, it will produce a boil, an osteomyelitis, an ulcerative endocarditis, a septicæmia, a pyæmia, etc.; the diverse manifestations produced by it are dependent both upon the general soil where it evolves and upon its localization.

We have already said that we must not take as synonyms the expressions " infectious agents " and " microbic agents." Infectious diseases may be produced by beings which are very different from the standpoint of natural history.

They may be classed in four categories:

1. BACTERIA, which belong to the family of algæ, and come under the group of *schizomycetes* (Nägeli), or, better, *schizophycetes.*

2. PATHOGENIC FUNGI, or *hyphomycetes*, of which the most interesting are represented by *aspergillus* and *streptothrix*. The latter form a transition between fungi and bacteria. Actinomyces is arranged here, and there is a tendency now to include also the agent of tuberculosis.

3. PATHOGENIC YEASTS, or *blastomycetes*, which, however, could find their place in the group of fungi.

4. ANIMAL MICROBES, and particularly protozoa.

Cultivation of Infectious Agents.—The majority of these pathogenic agents may be isolated and cultivated on artificial liquid or solid media.

As liquid media, mineral solutions have been used, for which a good many formulæ have been given since the first researches of Cohn and Nägeli. Vegetable infusions may also be employed, and liquids prepared with hay, straw, barley, malt, etc., are often utilized. In most cases we have recourse to animal substances; we use bouillon with or without peptone. Preference is sometimes given to natural products, such as defibrinized blood, serum, urine, milk, acetic fluid, aqueous humour, the white of egg, and the like.

The second procedure consists in cultivating microbes on solid media. A vegetable or animal infusion is taken and solidified by the addition of gelatine; this solid medium liquefies at 23° C., and therefore it can not be placed in the incubator. In order to make cultures at a temperature of 37° to 38° C., we replace gelatine by another substance, agar-agar.

In the case of strongly albuminous natural liquids it suffices, in order to solidify them, to coagulate them by heat. This is what is done with blood serum, defibrinized blood, and the white of egg.

Finally, we frequently utilize slices of cooked vegetables, such as potatoes, carrots, artichokes, etc.

The media may also be modified by the addition of various substances—e. g., glucose, glycerine, aniline colours, and tincture of litmus.

When the agent under study has been deposited on the medium adapted to it, the culture may be left alone at the surrounding temperature. Usually it is put into incubators regulated at 37° or 38° C.

According to the element under observation, cultures are made with free access to air or protected from air. In the latter case use is made of tubes from which the air has been extracted by means of a pump, or which have been filled with an inert gas. It is often sufficient to cover the medium with a layer of sterilized oil, or simply to deposit the microbe at the bottom of a tube containing a sufficient amount of agar-agar. The air does not penetrate into the deep parts. Finally, one may resort to an arrangement which permits the absorption of oxygen by pyrogallic acid.

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Division of Bacteria.—The various procedures above indicated permit the cultivation not only of bacteria, but also of the majority of fungi and yeasts. In general, cultures are not attended with success in the case of animal microbes, except, perhaps, the amœbæ.

In order to determine what kind of microbes we are dealing with, we must take into account a whole series of characteristics. With few exceptions, the appearance of the colonies upon a medium is not sufficient; we must multiply and vary the cultures, and complete, by microscopic examination and inoculation in animals, the first results thus obtained.

Since the researches of Weigert, Koch, and Ehrlich, it is customary to stain microbes with aniline colours. The reactions produced by colouring matters may serve in diagnosis. There are microbes which re-

FIG. 4.—Schematic aspect of the various species of bacteria. *A*, monococci; *B*, diplococci; *C*, streptococci; *D*, tetracocci; *E*, staphylococci; *F*, bacilli; *G*, bacteria; *H*, leptothrix; *I*, cladothrix; *J*, spirilla.

tain them strongly; others part with them readily. Several are easily discolorized by alcohol, after the action of iodo-iodide reagent; this is what constitutes Gram's method.

Microbes have been classified most often after their morphological aspect. Now, when less importance is attached to morphology than formerly, the old classifications have been simplified. There are now but two great groups admitted: sphero-bacteria, called cocci or micrococci, and staff-shaped bacteria, called bacilli or rods.

Micrococci are small spheres, which are generally nonmotile, unprovided with vibratile flagella, reproduced by fission, and bear no spores.

Bacilli are small rods, often motile and provided with vibratile

cilia, reproduced by fission and often by sporulation. Generally sporulation occurs in the form of endospores, seldom of arthrospores, which are distinguished by their remarkable refracting power and their great resistance to colouring reagents.

According to their groupings (Fig. 4), micrococci have been divided as follows:

1. *Monococci*—presenting themselves under the form of small spheres well isolated from each other.

2. *Diplococci*—consisting of two cocci, joined.

3. *Streptococci*—more or less long chains, consisting of 3 or 4 to 40 or 50 individuals; their appearance may be compared to a pearl necklace.

4. *Tetracocci* or *tetragenus*—formed of four cocci or tetrads, and placed on the same plane.

5. *Sarcinæ*—in which the division is made in all directions. These are small cubes having four cocci on each side.

6. *Zooglea*—represented by masses of micrococci united by a sort of jelly.

7. *Staphylococci*—a variety of zooglea presenting the aspect of grape bunches.

Bacilli have frequently been divided into three groups:

1. *Bacilli*, properly so called—slender rods and often motile.

2. *Bacteria*—larger rods.

3. *Bacteridia*—large and nonmotile rods. The anthrax bacillus comes under this group.

However, though we say "anthrax bacteridium," the distinctions that we have just indicated are no longer admitted to-day. The generally admitted classification is as follows:

1. *Bacilli*, properly so called.

2. *Leptothrix*—long, segmented filaments.

3. *Beggiatoa*—long, thicker filaments.

4. *Cladothrix*—bacteria which appear branched. In reality the branchings are false. The elements, being born by fission, remain close side by side at their points of origin, the primitive element continuing to grow. One might believe, at first sight, that there is a lateral ramification.

5. *Spirilla*—curved bacteria receiving sometimes the name of *vibrios*, when the element is bent, and spirilla when the microbe represents a rolled filament. The term *spirochæta,* applied to long and flexible spirilla, is now abandoned.

Variations of Bacteria.—The classification of bacteria is, as can be seen by these examples, based entirely on their forms. It would have been a good one if the forms were invariable. But such is not the case.

The doctrine of monomorphism, supported by Cohn, had to give way to the conception of polymorphism developed by Nägeli and supported by Pasteur. It is to-day a familiar truth that the form of bacteria, especially of bacilli, is being constantly modified; the same is true of other pathogenic vegetables. Streptothrix and yeasts present, according to a great number of circumstances, very marked variations.

In this respect, two orders of modifications are to be distinguished.

Microbes change their form at certain periods of their development; such is the case with the colon bacillus, which presents itself first under the form of filaments, then of rods, and finally of oval elements, short enough to simulate micrococci. Modifications no less notable are observed in old cultures where certain elements, often swollen into a club shape, constitute what are called *involution forms*.

In other cases, variations are produced because the medium has been changed. The anthrax bacillus forms small rods in the blood of animals and long filaments in culture media; soon these filaments inclose spores, while these organs of reproduction are never met with in the blood. Likewise, different forms are obtained by sowing microbes in diverse media, such as bouillon, agar-agar, or potato. Finally, adding small amounts of antiseptics, we may observe the development of new forms, which often do not at all resemble the primitive stock.

This polymorphism, though very well marked, is not surprising. It is a particular case of the great laws of evolution. The surrounding medium having changed, the being could not remain identical. Similar modifications are observed with certain yeasts, which, according to the media, appear under the form of oval elements or mycelial filaments. The same variations are also noted in the case of actinomycetes, which at one time are composed of masses of radiate filaments terminating in club form, and at another arranged in the forms of small rods similar to bacilli. A still more curious example is furnished by the tubercle microbe, which under certain conditions offers morphological characteristics that have sometimes led to its being considered a streptothrix akin to actinomyces.

Certain bacteria possess the property of being surrounded by a capsule. This is the case with pneumococcus, pneumobacillus, and tetragenus. But this characteristic is not any more constant than the others. Bacteria lose their capsules in certain media; some may acquire them accidentally, as does, for instance, the streptococcus.

The sporogenic property is not any more fixed. By certain con- . trivances there are created new races, called asporogenic. The bacterium of anthrax, after being cultivated in bouillon to which chromate

of potassium is added, loses its sporogenic property in the following generations, even if it be replaced in ordinary media.

Under the impulse of Pasteur's ideas, it was thought that a basis of classification could be found in the study of fermentations produced by microbes. Many objections may be made to this view. Let us take, for instance, the colon bacillus. Here is an agent which engenders lactic acid and indol. There exist microbes having the same biological characters, but which do not produce these fermentations. Chemists look upon them as different species, and the majority of bacteriologists make of them simple varieties, under the name paracolon bacilli. What gives a certain amount of support to this opinion is that modifications may occur in the fermentative power of certain samples; there are cases on record where a paracolon bacillus, after a series of cultures in artificial media, has acquired the ability to produce lactic acid and to coagulate milk.

Nor can we classify microbes on the basis of their chromogenic function. Some of them produce various pigments—green, red, yellow, violet; but, by placing them under unfavourable conditions, by submitting them to high temperatures, to the influence of compressed oxygen, or to the action of antiseptic substances, it is possible to suppress this function, sometimes permanently.

A final characteristic remains, and the most important from a medical point of view. Microbes have been divided into three groups—*saprophytes, parasites,* and *pathogenics*. Saprophytes are those which multiply on dead matter; parasites exist on living beings, without notably harming them. The pathogenics provoke the development of diseases. This distinction is not yet absolute. Certain saprophytes, falling accidentally on a living organism, may, so to speak, become accustomed to this new medium and rise to the rank of parasites or of pathogenic agents. The parasites that we bear on our bodies are equally modified by a great number of circumstances. The exaltation of our habitual guests is one of the principal causes of infectious diseases, and, *vice versa*, the most virulent agents lose, at certain moments, their pathogenic action and revert to the rank of parasites and saprophytes. It is exactly upon these functional variations that the great principle of the attenuation of viruses and of vaccination is based.

Lastly, we must remember that cultures are never homogeneous. Microbes, as living beings, have their individuality. In any given colony there are always certain individuals more fully developed or more resistant than others. This explains why small doses of antiseptics do not kill all microbes at the same time, but only decrease their number; it is the weakest that perish. In the same way a colony of

chromogenic microbes largely spread on a nutrient surface will give birth to new colonies, some of which will be deeply coloured and some colourless. The same remarks are applicable to pathogenic properties. Functional variations, attenuations, and exaltations are individual modifications.

We shall therefore conclude that, in order to determine the species of a microbe and its place in the classification, we must pursue very long investigations, because we must take into account a whole series of characters. We must thoroughly study its morphology, its reactions toward colouring reagents, the appearance of its cultures on various media, its fermentative properties, and its pathogenic action. It is only upon the *ensemble* of the properties of a microbe that a conclusion can be founded. Still, in certain cases, it will be impossible to decide and to recognise the species under examination.

CHAPTER VI

ANIMATE AGENTS (Continued)

The animal parasites—The vegetable parasites—The infectious agents—Bacteria: their division into specific and nonspecific—Phycomycetes—Mycomycetes— Protozoa—Medical classification of infectious agents.

WITHOUT having the intention of describing, even briefly, the parasites and infectious agents actually known, we believe it useful to indicate the species most frequently encountered, or at least those most interesting from a medical point of view.

ANIMAL PARASITES *

The animal parasites are all invertebrates, which enter into the group of annelida and that of protozoa.

Insects.—The parasite insects belong to the order of diptera or hemiptera.

DIPTERA.—Among the diptera we shall simply note the flea, the chigoe, the œstrum, and the muscides. The larvæ of certain insects may live beneath the skin or in the natural cavities of man. The best known of the skin larvæ are the moyoquil worm of Mexico, the macaco worm of New Grenada, and the Cayor worm. The cavity larvæ (*Lucilia macellaria, Sarcophaga magnifica, carnaria*) develop in the sinuses of the face and may produce very grave disturbances.

HEMIPTERA.—Hemiptera comprise the bedbug, and especially the louse, of which three varieties are admitted: the head louse (*Pediculus capitis*), the clothes louse (*Pediculus vestimenti*), and the crab louse (*Phthirius pubis*). The latter occasions, through a liquid which it secretes, the production upon the skin of slaty blue spots, peculiarly abundant when some intercurrent infection modifies the chemical constitution of the blood. Hence, these spots were first described in febrile diseases, and considered as an eruptive manifestation.

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* In preparing this chapter we have largely drawn from Dr. R. Blanchard's works on medical zoology.

It is very curious, from a point of view of general pathology, to note that these three species of lice live in determined regions, which they hardly ever leave. Evidently they find among the various parts of the body differences which we are unable to perceive.

Acarina.—The principal species, from a medical point of view, is *Sarcoptes scabiei,* the agent of scabies or itch.

This group comprises *ixodes*—the *Ixodes ricinus,* which is quite innocent, and the *Argas persicus,* which produces, it is said, grave lesions. The *Trombidium holosericum* produces a larva of a beautiful red colour, known under the names red flea, harvest bug, or *Leptus autumnalis,* which fixes itself beneath the skin and gives rise to small papules attended by intense pruritus. Recovery supervenes spontaneously in six or seven days. The *Demodex folliculorum* is frequently observed in the sebaceous glands, mainly in the ala of the nose; it is believed to be the cause of acne punctata.

The *linguatulæ,* which are now looked upon as degraded acarina, are encountered in man in two states. As adults, they may invade the nasal fossæ; in the larval state, they have been observed in the abdominal organs, and particularly in the liver.

Helminthes.—The great group of helminthes, so important from a medical point of view, comprises a large number of species, parasites of man. We present in the following table those that are most common.

PLATYELMINTHES.

Cestodes.

Tæniadæ.

Tænia solium.
"   saginata.
"   echinococcus.

Bothriocephalidæ.

Bothriocephalus latus.

Trematodes.

Fasciolidæ.

Fasciola hepatica.
Schistosomum hæmatobium.

NEMATHELMINTHES.

Nematodes.

Ascaridæ.

Ascarides lumbricoides.
Oxyurus vermicularis.

Strongylidæ.

Eustrongylus visceralis.
Uncinaria duodenalis.

Trichotrachelidæ.
　　Trichocephalus trichiurus.
　　Trichinella spiralis.

Filaridæ.
　　Filaria medinensis.
　　"　　sanguinis.

Angiostomidæ.
　　Strongyloides intestinalis.

Tænia solium, Tænia saginata, and *Bothriocephalus latus* represent the three great tapeworms of man. The bothriocephalus is the least common; it is mostly met with in the regions of the lakes of Geneva and Neufchâtel. In certain cases man is affected with elephantiasis, characterized by the development of numerous cysticerci occupying the subcutaneous cellular tissue, exceptionally the brain and the eyeball. As many as 2,000 tumours have been counted in one patient.

Tænia echinococcus is, when mature, a parasite of the dog, whose intestinal canal it inhabits. The eggs, swallowed by man, give birth to a hexacanth embryo, which penetrates into the organism, and, fixing itself in some organ or tissue, generally in the liver, produces a hydatid cyst. The latter grows, often reaching enormous proportions; but, although its contents include toxic substances, it acts chiefly in a mechanical manner, by compressing the neighbouring parts.

Fasciola hepatica, distoma of the liver, inhabits the biliary passages. It causes grave disturbances—pain, icterus, and a cachexia which finally ends in death.

There exists a very grave disease, bilharziosis, which is chiefly observed in Egypt, and is due to *Schistoma* or *Distoma hæmatobium, Bilharzia hæmatobia.* The parasite lives in the blood, on which it nourishes itself, but causes no disturbance; only it produces eggs provided with spurs, which, stopping in the capillaries, tear them, and give rise to very grave hemorrhages. These sometimes occur as hematurias (hematuria of Egypt), sometimes enterorrhagias. At the autopsy as many as 500 worms may be found in the portal system. The evolution is very long; it may persist for ten or fifteen years.

Of the nematodes, *Ascarides lumbricoides* represent, as is known, worms extremely common. They are often found in great numbers in the intestine, as many as 5,000 in a case recorded by Fauconneau-Dufresne. Generally well borne, they may produce accidents of a reflex or even febrile nature, accompanied by grave general manifestations, described as typhoid lumbricosis.

Oxyures are also very frequent. They are mostly met with in children, in the anus and the vulva, where they occasion intense itching.

Eustrongylus visceralis is a very rare parasite, inhabiting the urinary passages, whence it may be voided with the urine. It produces grave disturbances, notably hematuria.

On the contrary, *Uncinaria duodenalis* is very prevalent. It lives upon the intestinal mucous membrane, and there causes small hemorrhages. The latter, by their repetition, soon give rise to a quite grave anæmic condition. To this worm is to be attributed the endemic anæmia which is observed in miners (anæmia of St. Gothard, of the coal mines of the Loire, in the north of France), and in those working in rice fields or in clay.

We shall not dwell on the *trichocephalus*, which is frequently found in the digestive canal, where it is introduced through the drinking water. Generally inoffensive, it sometimes produces quite serious reflex phenomena.

Otherwise important is *Trichina spiralis*, which produces the disease known under the name *trichinosis*. Man is infected by eating insufficiently cooked pork. The parasites at first multiply in the intestine and produce diarrhœa and general disturbances resembling those of typhoid fever. Then they penetrate by the chyliferous vessels, invade the mesenteric glands, pass into the thoracic duct, reach the blood, and, after passing through the lung, arrive at the capillaries; others penetrate directly from the intestine into the blood, and yet others pass through the walls of the alimentary canal. The trichinæ then become encysted in the muscles, and, in case they attack the respiratory muscles in great numbers, they bring about a fatal termination by asphyxia. While of very frequent occurrence in Germany, trichinosis is exceptional in France.

The *threadworm of Medina* produces a disease called *dracontiasis*, characterized by the production of abscesses affecting particularly the legs and feet. When the abscesses are opened, one may see the parasite rolled up at the bottom of the wound. It may be extracted by drawing it out and coiling it around a small stick. The operation should be done with great care, for the rupture of the worm, probably giving issue to a toxic substance, is followed by very grave disturbances.

The name *Filaria sanguinis* is a collective term applied to diverse filariæ living in the human blood. These parasites are encountered exclusively in hot countries. A great number of species are recognised, the four principal ones being *Filaria nocturna* or *Bancrofti, Filaria diurna* or *loa, Filaria perstans,* and *Filaria Demarquayi.*

Filaria nocturna lives in the lymphatic vessels; it produces lymphatic abscesses on the limbs, lymphatic tumours in the scrotum, and, according to Manson, elephantiasis of the Arabs. *Filaria diurna* lodges itself ordinarily between the conjunctiva and the eyeball.

Filaria perstans produces a peculiar affection, observed in negroes and described under the name " sleeping sickness."

Strongyloides intestinalis is observed in patients suffering with the diarrhœa of Cochin China.

Protozoa.—Very numerous parasites belonging to the group of protozoa may be met with in man.

We find, first, among the *infusoria, Balantidium coli,* which is encountered in diarrhœal stools. This parasite has been seen about forty times, but it has never been encountered in France.

Flagellata comprise three interesting species : *Cystomonas urinaria,* found in the urine; *Trichomonas vaginalis,* which is very common, and has been met with in the vagina, the bladder, the alimentary canal, and in the expectorations of patients suffering with pulmonary gangrene; and *Cercomonas* or *Lamblia intestinalis,* which vegetates also in diarrhœal matter.

We shall leave out of consideration for the present the other protozoa, the coccidia, hemosporidia, and rhizopoda, since all that is important to know about them will be treated of in connection with infections.

Vegetable Parasites

Among vegetable parasites, we shall note, first, those concerned in the production of *tinea.* These are *Trichophyton tonsurans,* the agent of tinea tonsurans, herpes zoster, and parasitic sycosis, and *Achorion Schönleinii,* the agent of favus. The study of these fungi has been pursued with great care in recent years, especially by Sabouraud, Sabrazes, and Bodin, who have well shown the necessity of dividing them into a great number of species upon which we do not need to dwell here.

Then comes the group of *microsporon,* comprising the *Microsporon furfur,* the cause of pityriasis versicolor; the *Microsporon Audouini,* to which alopecia is attributed; the *Microsporon minutissimum,* which is found in erythrasma; and the *Microsporon anomœon,* which produces pityriasis circinata.

The other vegetables which we must now study may live under three different states. They are, according to circumstances, saprophytes, parasites, or infectious. We shall take them up when studying infectious agents. We shall only note them here.

These vegetables are divided into two groups : Mycomycetæ, comparatively high fungi, and Phycomycetæ, which constitute a transition between fungi and algæ.

Among Mycomycetæ we find *aspergillus* and *eurotium, penicillium* and *blastomycetes,* or *yeasts.*

The PHYCOMYCETÆ include the important group of *mucors*. *Mucor niger* produces on the tongue a very tenacious black coating. The *Mucors corymbifer, septatus,* and *ramosus* enjoy with *Aspergillus fumigatus* and *flavus* and *Eurotium repens* and *malignum* the property of living as parasites. They are often met with in the auditory canal, where they give rise to the affections grouped under the general name otomycosis.

Let us note also *Cercosphæra Addisoni,* which is found in various skin diseases and in certain alopecias.

Finally, there have been described under the name *leptomitus* parasites which are divided, according to the point of the organism where they were encountered, into leptomitus of the epidermis, of the urine, of the uterus, of the vagina, and of the aqueous humour.

INFECTIOUS AGENTS

Bacteria.—While bacteria are not the only parasites capable of producing infections, they incontestably hold the first place and represent the true types of infectious agents.

Their number is so considerable that we can not study all of them. We shall only note the principal species.

According to the division which we have already admitted, we shall successively consider the *micrococci* and the *bacilli,* and in each group we shall study the common *nonspecific* and *specific* species.

Nonspecific Micrococci.—The nonspecific micrococci are not very numerous. It suffices to know four of them: staphylococcus, streptococcus, pneumococcus, and tetragenus.

STAPHYLOCOCCUS (Rosenbach, 1884), the most prevalent of all, is represented by small rounded elements, measuring from 0.7 micron to 1.2 micron, sometimes isolated, oftener united. They assume the form of diplococci when they are developed in a liquid medium. If we take a particle of a colony vegetating on some solid medium, we see that the grains form masses that have been compared, more or less exactly, to bunches of grapes. Hence the name given to this species. In many cases, however, the grains are in masses or in the form of long bands, sometimes even of small chains.

This microbe develops readily upon the various media employed in bacteriology. On agar-agar, it forms a thick, moist growth; gelatine is rapidly liquefied, and the bottom of the tube contains colonies united in flocculent masses. Bouillon becomes uniformly turbid and often contains a mucous deposit. Milk coagulates in about eight days. Solidified serum liquefies slowly.

The colour of the cultures varies notably according to circumstances. Therefore three great varieties of staphylococci have been

admitted: *Staphylococcus aureus,* producing on agar-agar and pota-
toes colonies of a superb orange-yellow colour; *Staphylococcus citreus,*
whose name sufficiently indicates the colour; and *Staphylococcus albus.*

It has long been a matter of discussion whether the three staphylo-
cocci represent distinct species or but varieties of the same species.
The latter opinion tends to prevail, since the different types are fre-
quently found associated in the same morbid focus and numerous
transitions are observed between well-differentiated samples. Finally,
by certain experimental contrivances, we may easily cause the *Staphy-
lococcus aureus* to lose its chromogenic power; it is thus transformed
into the white variety.

Staphylococci are found as saprophytes in soil, water, ice, air,
dust, and various objects. They vegetate as parasites upon our in-
teguments and mucous membranes, particularly upon the buccal
mucous membrane, less frequently upon that of the intestine. They
may penetrate into the excretory ducts of the glands; even in the milk
of healthy women, the white variety is almost constantly present.

When they attain the rank of pathogenic agents, staphylococci, in
most cases, give rise to suppurations. In general, it may be admitted
that the chromogenic varieties are more virulent than the white vari-
ety. According to the seat of the lesions and the activity of the germ,
the effects vary greatly. In some cases, simple acneform pustules are
observed; in others, boils or so-called carbuncle, or some affection
peculiar to hot climates, the *button of Biskra*; elsewhere, it may as-
sume the type of impetigo; at times, circumscribed or diffused phleg-
mons, sometimes even gangrene. When the deeper structures are
reached, suppurating foci will be observed either in the viscera or in the
tissues. Osteomyelitis, for instance, is, in most cases, due to *Staphy-
lococcus aureus.* In certain cases, instead of suppuration there is
destruction of the affected parts (ulcerative endocarditis). In other
cases, the infection becomes generalized; a number of microbic centres
are produced, ending in the formation of numerous small abscesses.
This is the purulent infection or pyæmia. If the microbe is very
virulent, no reactions are produced; the individual succumbs and the
necropsy reveals no lesions. This is the process known as septicæmia.

STREPTOCOCCUS, observed by Coze and Feltz, by Pasteur and Do-
leris, isolated from erysipelas by Fehleisen (1883) and from suppu-
rations by Rosenbach (1884), is a micrococcus measuring from 0.3 to
1 micron. They have the very characteristic property of grouping
themselves into more or less long chains. Some chains are made
up of 3 or 4 elements, others of 30 to 40, and present then the
form of a rosary or pearl necklace. In certain cases, diplococci
only are found; in others, the streptococci overlap each other and

agglomerate so as to form colonies which, on superficial examination, appear to be staphylococci. In general, all the elements of the same chain are of equal size; in certain cases, a few are more voluminous and break the uniform contour which is usually observed.

This microbe, a facultative anaërobe, produces on agar-agar small, slightly elevated, almost translucent, rounded colonies; the appearance is similar on gelatine, which is not liquefied. Bouillon is at first uniformly turbid, but soon becomes clear; the microbes fall to the bottom of the tube, where they collect into small granules or even small masses, which are readily scattered when the liquid is agitated.

The streptococcus develops readily on potatoes, but, as a rule, does not produce colonies visible to the naked eye.

Its action on milk is inconstant; in most cases this medium is coagulated by it.

The most luxuriant cultures are obtained in serum or in the liquid of ascites, either pure or mixed with bouillon; it is also in this medium that the microbe attains its maximum degree of virulence.

Like the staphylococcus, the streptococcus is widely distributed. It is found in the air, in water, and in the soil; it readily invades putrescible matters, and is frequently met with upon the skin, in the buccal cavity, where it is constant, and at times in the intestinal canal, where it inhabits mainly the duodenum.

This microbe may produce four orders of morbid manifestations: œdema, suppuration, pseudo-membranes, and gangrene.

Erysipelas is an inflammatory œdema *par excellence*; at times the dermatitis terminates at some points in the formation of small abscesses. This fact has been made use of to prove the identity of the streptococci of erysipelas and of suppuration.

Between exudative and suppurative inflammations we find lymphangitis, which occupies a position intermediate between erysipelas and phlegmon. Among the suppurative lesions we must mention the adeno-phlegmons, and particularly the diffuse phlegmons, which are nearly always due to streptococcus. When it is localized in the viscera, streptococcus still gives rise to the same lesions—e. g., in the kidney it produces an acute nephritis; in the lung, broncho-pneumonias; while in the other organs or in the serous membranes it causes more or less extended suppurations. If it attacks the inner coat of the circulatory system, it causes arteritis, phlebitis, and endocarditis, especially ulcerative endocarditis.

Finally, becoming generalized, it may, like the staphylococcus, perhaps oftener than the latter, produce pyæmia or septicæmia. Puerperal septicæmia is nearly always dependent upon the streptococcus.

The part played by the streptococcus in the formation of false

membranes has been well established by numerous observations of diphtheroid sore throats, in which this microbe is met with predominantly or almost exclusively. The same is true of other parts of the organism, notably of the vulva and vagina, which may in cases of puerperal infection become covered with false membranes caused by streptococcus.

Lastly, streptococcus may produce gangrene. This is observed in the patches of erysipelas, as well as in gangrene of the extremities consecutive to acute arteritis; the same microbe, it seems, may of itself provoke pulmonary gangrene, without the intervention of other germs.

Many authorities have admitted a great number of varieties or species of streptococci. The present tendency is to draw closer together and to unite the different species. It should not be forgotten, however, that different species are distinguished from each other by certain biological properties. It is well demonstrated, for example, that the serum of animals immunized against one variety of streptococcus often exerts no influence upon other varieties. Without concluding from this fact that there are specific differences, we must, nevertheless, admit that there are modifications sufficiently distinct to be expressed by peculiar biological characteristics.

The third micrococcus that we must mention is the PNEUMO-COCCUS. It was discovered in pneumonia by Talamon, thoroughly studied by Fraenkel, who identified it with the microbe of sputum septicæmia of Pasteur, Vulpian, and Sternberg, and subsequently by Weichselbaum. The pneumococcus is designated in France under the name of Talamon-Fraenkel, in Germany as *Diplococcus pneumoniæ* (Fraenkel), and in Austria as the Fraenkel-Weichselbaum diplococcus. It has been called by Gamaléia *Streptococcus Pasteuri*.

This microbe presents itself under the form of small lanceolate granules, comparable to the grains of barley, measuring from 1 to 1.5 micron. It is sometimes isolated, oftener united in pairs or in short chains, comparable to those of streptococcus (*Streptococcus pneumoniæ*). The individual cocci are remarkable for the clear capsule that surrounds them. This capsule is especially apparent when the microbe is developed in a medium rich in albumin—viz., in the living organism and in the blood serum.

More delicate than the preceding species, the pneumococcus does not develop at ordinary temperature; its development begins at about 24° C. On solid media, such as agar-agar or gelatinized serum, it gives rise to minute colonies resembling dewdrops, scarcely visible to the naked eye. Gelatine is not liquefied. In bouillon extremely small granules are observed. The best media are represented by blood serum, and particularly defibrinated blood, coagulated by heat. On the latter

medium, proposed by Gilbert and Fournier, the microbe develops luxuriantly and decolourizes the colouring matter of the blood, which is changed from brown to yellowish white. This phenomenon appears to be characteristic.

The pneumococcus, though somewhat less widely distributed than the preceding microbes, has been encountered in the air and in dust, but it is a parasite rather than a saprophyte; 20 out of 100 healthy individuals harbour it in their saliva. It may also be found in the nasal mucus and even in the intestine.

First encountered in fibrinous pneumonia, pneumococcus may produce, even in the respiratory apparatus, very diverse affections—broncho-pneumonias and bronchites. It frequently induces suppuration in the serous membranes: meningitis, pericarditis, pleurisy, peritonitis, which are characterized by the presence of thick, greenish, semi-solid exudations, extremely rich in fibrin. It may also produce arthritis, otitis, parotiditis, and localize itself upon the endocardium and cause vegetative or ulcerative endocarditis. Less frequently it invades the whole organism and induces septicæmia.

Very closely related to, if not identical with, the pneumococcus is *Micrococcus intracellularis meningitidis*, which is the cause of cerebrospinal meningitis.

Of late, attention has been drawn to TETRAGENUS (*Micrococcus tetragenus*, Gaffky, 1883). Morphologically, it is made up of 4 micrococci, united on the same plane and often surrounded by a capsule. It produces, in various media, moist, white colonies (a yellow variety also has been described). It does not liquefy gelatine; forms in bouillon a thick deposit.

This microbe is frequently met with in the mouth. It takes a prominent part in the development of "sore throats," in which, by cultivation on agar-agar, it is found in three fourths of the cases. From the buccal cavity, tetragenus may invade the neighbouring parts: in this way it causes dental abscesses and adeno-phlegmons of the cervical region; making its way into the ear, it produces otitis or mastoiditis. At other times, carried toward the respiratory apparatus, it produces a purulent bronchitis a pulmonary abscess, or contributes to the formation of tubercular cavities. Its presence has also been proved in cases of septicæmia and pyæmia, as well as in the urine of patients suffering with scarlatinal nephritis.

Nonspecific Bacilli.—At the head of the least of nonspecific bacilli is placed the COLON BACILLUS (*Bacillus coli communis, Bacterium coli commune*). discovered by Escherich. Very variable in its morphology, the colon bacillus presents itself sometimes under the form of small, motile rods measuring from 2 to 4 microns; some-

times under that of oval elements, which might easily be mistaken for micrococci, and at times under the form of quite long filaments. It is a facultative anaërobic motile bacillus, provided with from 4 to 10 vibratile ciliæ. It develops readily between 15° and 46° C. in all the media employed in bacteriology. On agar-agar or serum it forms a whitish layer; on gelatine, ovoid, transparent, or opaque colonies, which do not liquefy the medium. Potato is covered with a thick brown coating, and artichoke assumes a beautiful greenish tinge. Milk, in consequence of the fermentation of the lactose, becomes acid and coagulates more or less rapidly. Bouillon becomes uniformly turbid, and quite often contains little flocculi; in peptonized bouillon notable quantities of indol are formed.

On the various media the cultures emit a disagreeable odour, sometimes recalling that arising from decomposed urine, sometimes that of putrefaction.

Gas is sometimes abundantly produced in milk, potatoes, and gelatine. It is then due to a variety long considered to be a particular species—namely, *Bacillus lactis aerogenes.*

Certain varieties of colon bacilli do not ferment lactose or produce indol; these are called paracolon bacilli. Experimenters have several times succeeded in inducing, by serial cultures in milk, the fermentative power, which was previously lacking.

The colon bacillus is a very prevalent microbe, perhaps the most widely distributed of all. It is found in the air, soil, and water, and it is constantly met with in the alimentary canal of man and of animals, in the mouth, in the stomach, and particularly in the intestine. Discharged with the fæcal matter, it readily soils the external genitals, where its presence is also almost constant. In certain animals it affects the mammary glands, as is notably the case with the cow; hence, the colon bacillus is encountered in the milk, where Pasteur described it under the name *lactic ferment.*

When this microbe attains virulence, it produces very various lesions. It is the principal agent of intestinal infections—e. g., acute or chronic enteritis, infantile cholera, cholera nostras, colitis, and appendicitis very frequently depend upon it. In cases of dysentery of hot countries, and at times in dysentery nostras, the stools contain in great abundance a variety of colon bacillus which has been considered the cause of the disease. From the intestine the microbe may make its way to the excretory ducts, and produce suppuration in the biliary passages or inflammation in the pancreas; or else, passing through the walls of the intestine, it gives rise to peritonitis; or, again, passing by the portal vein, it localizes itself in the liver, and there induces infections, degenerations, and often grave icterus.

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Less frequently it acts in the mouth, produces sore throat, or reaches the neighbouring parts, notably the parotids.

While it assumes a very important rôle in intestinal pathology, its etiological significance in urinary pathology is by no means inconsiderable. It produces cystitis, and may spread from the bladder toward the kidney, where it frequently induces lesions terminating in renal insufficiency. It is the great agent of death in patients suffering from urinary disorders.

Lastly, in women, it has several times produced a variety of puerperal septicæmia.

It must be remembered that, in order to affirm that a certain lesion is due to the colon bacillus, it does not suffice to prove its presence in the cadaver. After death, or rather during the agony, the colon bacillus often leaves the alimentary canal, particularly in those cases where the intestine has suffered alteration or ulceration, and invades the other organs, especially the liver.

It has not always been possible to refer to the colon bacillus group the microbes encountered in the various lesions above mentioned. Therefore authors have described as distinct species a whole series of agents, which are at present identified. Besides the *Bacillus lactis aerogenes* and the lactic ferment, which we have already noted, we must class with the group of colon bacilli *Bacillus neopolitanus*, found by Emmerich in the organs of cholera subjects, *Bacillus pyogenes fœtidus* of Passet, the septic bacterium (Clado), and the pyogenic bacterium (Albarran and Hallé) of urinary infections, the bacillus of dysentery of Chantemesse and Widal, the bacillus of ulcerative endocarditis of Gilbert and Lion, etc.

We may also class this microbe with the *bacillus of psittacosis*, described by Nocard, Gilbert, and Fournier. This is a microbe very common among parrots, and produces in man extremely grave bronchopneumonia.

Some authors consider as a variety of colon bacillus the *pneumobacillus of Friedländer*, which should not be confounded with the pneumococcus. It differs from the colon bacillus by the presence of a capsule, which, however, is not constant. It produces in man sore throat, broncho-pneumonia, and septicæmia.

Another septicæmic agent, *Bacillus septicus putidus*, encountered for the first time in a patient dead of septicæmia consecutive to cholera, deserves to be placed close to colon bacillus. It clearly differs from the latter by a very important characteristic: it liquefies gelatine. Pathogenic for animals, it has served for various experimental investigations.

Three other nonspecific bacteria may be met with, which are of

great importance in experimental and comparative pathology. These are the *bacillus of hemorrhagic septicæmia, Proteus vulgaris*, and *Bacillus pyocyaneus*. The latter, discovered by Gessard in 1882 and well studied by Charrin, possesses the interesting property of engendering a blue colouring matter, pyocyanin, which may be obtained in a crystalline state.

Leptothrix.—In the group of leptothrix we shall only mention *Leptothrix buccalis*, which may produce in man anginas (pharyngomycoses) of a particular character, abscesses, and even invade the economy.

The characteristic common to the various bacteria thus far noted lies in the fact that all produce analogous inflammatory processes. The dominant feature, from a clinical point of view, is the localization. The evolution of the morbid phenomena, their innocence or gravity, is dependent upon the tissue or organ attacked and upon the extent of the parts involved. Finally, these same agents may invade the economy, causing septicæmia or pyæmia, according as inflammatory reactions are present or absent.

Specific Micrococci.—The specific bacteria comprise but two micrococci.

The best known is the microbe of gonorrhœa, the Gonococcus, discovered by Neisser in 1879. The appearance of this coccus is quite characteristic. In examining the pus of gonorrhœa, we find the gonococci made up of two segments coupled, presenting somewhat the form of two beans, arranged with their concave surfaces toward each other. These microbes lie free or are inclosed within pus cells or epithelial cells; in most cases the same cell incloses a great number of them. They are not stained by Gram's method, and this fact serves to differentiate them from the common pus cocci.

The cultivation of gonococcus is a matter of difficulty. For a long time human blood serum was used as a medium. At present it is known that this coccus may develop in the serum of the rabbit; upon glycerine agar-agar, where it forms white, thin, transparent colonies; or on potatoes, where it produces minute drops.

This microbe causes a specific suppuration in the urethra, in the vagina, and at times in the rectum, the nose, and the conjunctiva. It is the usual causative agent in purulent ophthalmia of the newborn.

In cases of urethral or vaginal gonorrhœa, the gonococcus manifests hardly any tendency to leave the genital mucous membranes. Even though it locates itself with great tenacity in the cells and the glandular crypts, it only exceptionally invades the neighbouring glands, and but rarely enters the blood. The complications of gonorrhœa, the arthropathies, are due to secondary infections. In most cases

the gonococcus simply opens the way to the common pyogenic bacteria. The rheumatism of gonorrhœa must be considered as an attenuated pyæmia. Gonococcal arthropathies do exist, but they appear to be rare, although they are more frequent than was formerly believed.

The second specific micrococcus has been little studied; it is the MICROBE OF MUMPS, described by Laveran and Catrin.

The Specific Bacilli.—The specific bacilli are more numerous. There are thirteen of them, of which ten are aërobic and three anaërobic.

The specific aërobic bacilli are headed by the BACILLUS ANTHRACIS (*bactéridie charbonneuse*), discovered by Davaine in 1850. The latter is found in the blood of animals which have succumbed to the disease. It appears in the form of small nonmotile rods, measuring from 5 to 6 microns in length and 1 to 1.5 micron in breadth; the rods are sometimes surrounded with a capsule, and the ends are cut at right angles and slightly sinuous. In artificial media, particularly in liquid media, these rods become elongated in the form of segmented filaments, often very long, which soon produce spores. Spores are never found in the animal organism or in cultures grown in blood serum.

Bacillus anthracis readily develops in the presence of oxygen. It grows between 10° and 45° C. On agar-agar it gives rise to white colonies, on gelatine to granular colonies, which rapidly liquefy the medium and form a deposit analogous to a mass of rolled thread. Potatoes becomes covered with a thick coating. Bouillon, at first turbid, later becomes clear, the microbes falling to the bottom of the tube in the form of dense white flocculi.

The action on milk is quite variable. If the milk is put in a tube, the bacillus, living only in the upper layers, secretes a casease, which is diffused and produces coagulation. If, on the contrary, aeration is ample—viz., if the milk is put in a large vessel, at the bottom of which it forms a thin layer—the casein is digested and transformed into peptone as fast as it is coagulated; the milk assumes the character of a thick and brownish liquid.

Owing to the nature of its spores, *Bacillus anthracis* easily resists destruction. It persists for a very great length of time in the soil and water, thus causing very deadly epidemics and epizooties.

We must recognise, however, that in most cases contamination takes places otherwise. Man is most often affected in dealing with the cadavers of anthrax animals, or by manipulating the products derived from them—wool, horns, skin, etc.

Another bacillus, which also plays a part in man and animals, is the BACILLUS OF GLANDERS, *Bacillus mallei*, well described by Loeffler and Schutz in 1883.

This organism occurs in the form of long, slender, motile rods, measuring from 2 to 5 microns, often inclosing in their interior feebly coloured vacuoles. They grow very readily on agar-agar with glycerine; in bouillon, in which they form a viscous precipitate, and on potatoes, on which they produce a thick coating of a greenish-blue colour, the appearance of which is almost characteristic.

The disease generally attacks the horse, which transmits it to man. The feeble resistance of the microbe explains why direct contagion is observed as a rule.

The TYPHOID BACILLUS, described by Eberth in 1880, presents itself in the form of cylindrical rods, measuring 0.6 to 1 by 2 to 4 microns. In old cultures it produces filaments and forms of involution.

In many respects this microbe resembles the colon bacillus. It differs from it in certain important characters. It is more motile, this being due to the fact that it is provided with a greater number of ciliæ, 8 to 24. Colonies on agar-agar and gelatine are more transparent; on potatoes they are hardly visible, or form a light, whitish coating. Contrary to the colon bacillus, the typhoid bacillus does not yield a green colour when cultivated on slices of artichoke. It produces no indol in peptonized bouillon, does not ferment lactose, or coagulate milk. It resists much less the action of antiseptics—carbolic or arsenious acid.

However, these characteristics have not an absolute value; in the group of paracolon bacilli are found numerous species which seem to establish an insensible transition between the bacillus of Eberth and that of Escherich.

A final characteristic, derived from serum reaction, has lately been spoken of. It has been noted that the serum of animals immunized against the typhoid bacillus, or that of individuals attacked by typhoid fever, agglutinates the typhoid bacillus, but never the colon bacillus. This fact, although disputed, is interesting; but it is not of such great value as might be supposed, for similar reactions are observed with varieties of one and the same species. This is what occurs notably with the cholera vibrios.

It is then conceivable that several authorities persist in believing that the typhoid bacillus is but a variety of the colon bacillus. This theory, enunciated and sustained by Rodet and G. Roux, has appeared very seductive, for it explains the cases in which typhoid fever is generated spontaneously—that is, without any contagion. However, the idea of the specificity of the typhoid bacillus has just found a new argument in the researches of Reumlinger and Schneider. These authors have proved that the typhoid bacillus is met with in the intes-

tines of normal individuals. It might then bring about the disease on the occasion of debilitating causes, and notably of overwork. Thus excited, it produces a case which is apparently spontaneously developed, and it becomes the starting point of an epidemic which is propagated through contagion.

Infection takes place mostly through the agency of water, exceptionally through the soil or the air.

The aqueous origin of typhoid fever is no longer questionable. Numerous observations have established that the disease undergoes recrudescence when the drinking waters are polluted, and diminishes when hygienic measures are enforced. The precautions taken in recent years against unhealthful water are therefore praiseworthy; but if observations are very conclusive, experiments are much less so. The difficulty of distinguishing the typhoid bacillus from the colon bacillus does not enable one to admit the majority of analyses in which the typhoid bacillus is said to have been found in the water. The colon bacillus exists in all waters, and thus renders researches very difficult. This is what resulted from an experiment of Grimbert: This author introduced into 1,000 cubic centimetres of water 1 cubic centimetre of a culture of the colon bacillus and 1 cubic centimetre of a typhoid culture. He agitated the mixture and showed that it is impossible to recover the typhoid bacillus or to isolate and differentiate it from the colon bacillus.

The BACILLUS OF DIPHTHERIA, observed by Klebs in 1883, and fully described by Loeffler in 1884, is a nonmotile rod, straight or rounded, measuring 0.7 by 2.5 to 3.5 microns. The elements are isolated or united in couplets, often well aligned, and, as is said, placed in range of battle. In old cultures we frequently meet with involution forms presenting the contour of clubs or spindles.

The diphtheritic bacillus develops at a temperature of about 24° C.; its growth is arrested at 42° C. and is particularly luxuriant between 35° and 37° C. On agar-agar quite distinct colonies or grayish streaks are seen; on gelatine, small spherical colonies; in bouillon, masses that fall to the bottom of the culture tube. The bacillus does not develop on potatoes. The most characteristic cultures are obtained by inoculation upon gelatinized blood serum. At the end of twelve hours the nutrient medium, maintained at 38° C., is covered with small white or gray colonies, about the size of a pin's head. It is, as is known, by means of cultures on serum that one can readily establish the bacteriological diagnosis of diphtheria.

This microbe may be encountered as a saprophyte, a parasite, or a pathogenic agent. As a saprophyte, it may live in dung and rags; as a parasite, it vegetates in the buccal cavity of healthy individuals;

as a pathogenic agent, it produces pseudo-membranous lesions, occupying generally the throat, invading the larynx and the nasal cavities, less frequently the conjunctiva, and exceptionally the bronchi. It may also attack other mucous membranes exposed to the air, notably the genital mucous membrane or the skin.

Rapidly destroyed by the rays of the sun, the diphtheria bacillus retains its vitality for a very great length of time when sheltered from light. There are cases on record in which the clothing of a child dead with diphtheria was packed in a drawer, and when, a year or two later, it was taken out, caused the infection to reappear.

The BACILLUS OF INFLUENZA OR GRIPPE, discovered by Pfeiffer in 1890, is one of the smallest that is known; it is a nonmotile, rectilineal rod, 0.5 micron long, separate or in chains of three or four elements. It develops upon agar-agar covered with a layer of the blood of man or of the pigeon, in the form of small, homogeneous colonies, visible only under a magnifying glass. The growth is somewhat more abundant on glycerine agar-agar; in bouillon with blood it assumes the form of small flocculi.

We now come to one of the most important microbes—namely, the TUBERCLE BACILLUS—discovered by Koch in 1882. This bacillus occurs in the form of nonmotile rods, from 2 to 4 microns in length. The bacilli possess a tinctorial reaction altogether characteristic. They are penetrated with great difficulty by the aniline colours. One must employ energetic mordants and leave the microbes in the colouring bath during twenty-four hours, or else heat the liquid until it gives off vapours; the staining is then produced within a few minutes. Once stained, the microbes retain the dye tenaciously, resisting the action of nitric acid in the proportion of one third, which decolourizes the other bacteria. They appear alone in preparations thus treated.

The tubercle bacillus readily develops in blood serum, in bouillon and agar-agar mixed with glycerine or various sugars, and on potatoes with glycerine. On solid media it forms dry or slightly moist scales; on liquid media, scaly, wrinkled films or pellicles, which, at the end of a certain time, fall to the bottom of the culture tube.

Recent researches demonstrate that in certain conditions the tubercle bacillus undergoes remarkable morphological modifications. Projections and ramifications appear, which at times terminate in club-shaped swellings. The microbe is therefore much more highly organized than was at first believed. But no conclusion has as yet been reached as to its proper position in botanical classification. Some authors, considering the lateral buddings as true ramifications, place it in the group of streptothrix, by the side of actinomyces. Others, arguing that the ramifications are false, class it among the bac-

teria, in the group of cladothrix. It is at times considered to be referable to a somewhat special kind, that of crenothrix. To conform to usage, we have left the agent of tuberculosis among the bacteria. If it finally be ranked with streptothrix, this would be the best argument against those who still maintain that all infectious diseases are of bacterial origin.

The tubercle bacillus is remarkable for its high pathogenic power. It attacks equally man, mammalia, birds, and even cold-blooded animals—the ophidia and fish. As in the case of many other microbes, there exist several varieties of tubercle bacilli. Three principal varieties have been described: (1) The bacillus of human tuberculosis, which is met with in man, mammalia, and, among the birds, in parrots; (2) the bacillus of avian tuberculosis, which attacks particularly the gallinæ; (3) the bacillus of fish tuberculosis. Struck with these differences, some authors claimed to see in these three agents three distinct species. At the present day all have agreed to consider them simply as varieties that may. be transformed one into the other.

The tubercle bacillus is endowed with a very great vitality and easily resists causes of destruction. This fact alone explains its great prevalence. None of the mammalia are entirely immune to it. It is the veritable scourge of our epoch. In Paris tuberculosis is responsible for 4.9 deaths out of each 1,000 inhabitants; in cities with less than 5,000 souls the figure is 1.81. Among animals, the bovine species are the most frequently attacked. Contrary to popular opinion, tuberculosis is of very frequent occurrence in the domestic carnivora, notably in the dog (Cadiot).

Tuberculosis may be transmitted from animals to man. More frequently infection takes place from man to man, and may give rise to true epidemic centres. In the majority of cases inoculation occurs in the respiratory passages; it is through the sputa that the bacilli are transmitted. They represent a real social danger against which a struggle has justly been inaugurated in recent years.

The other pathogenic bacilli are less important for our studies; they require but brief mention.

First is the BACILLUS OF LEPROSY, discovered by Hansen, whose morphological and tinctorial characteristics are quite analogous to those of Koch's tubercle bacillus.

Let us mention the BACILLUS OF PLAGUE, recently discovered by Yersin and Kitasato; a bacillus analogous to the colon bacillus, described by Sanarelli, under the name *Bacillus icteroides*, as the agent of YELLOW FEVER; and a bacillus encountered by Roger and isolated by Lemoine and by Barbier and Tollemer from the stools of patients suffering from DYSENTERIFORM ENTERITIS. The latter bacillus is

very virulent; it can in certain cases give rise, in animals under experiment, to intestinal ulcerations analogous to those of dysentery and to hepatic abscesses. Lastly, the BACILLUS OF SOFT CHANCRE (Ducrey, 1889), a thick and short bacillus, often constricted in the middle, sometimes arranged in the form of chains, which no one has succeeded in cultivating.

Among the microbes thus far studied, several are facultative anaërobics. We have yet to mention three which vegetate only when excluded from air. These are the bacilli of tetanus, of gaseous gangrene, and of rheumatism.

The BACILLUS OF TETANUS or BACILLUS OF NICOLAIER (1884) is represented by very slender elements, from 2 to 5 microns long, motile, and generally provided with a large terminal spore, which gives them the appearance of pins. Sown on agar-agar and protected from air, they produce flocculent colonies and cause a liberation of gas, which splits the medium. Gelatine is rapidly liquefied and filled with gas bubbles. Bouillon is at first made turbid, but subsequently becomes clear, the microbes falling to the bottom of the tube, where they form a granular deposit. The culture has a very strong and disagreeable odour.

Owing to its spores, the tetanus bacillus is very resistant and very widely distributed. It is found in the soil, in mud, in dung, and dust; it is also met with in the digestive canal of herbivora, and is passed in abundance in their excreta. When it assumes pathogenic properties it develops at the point of infection, where it remains, and causes an intoxication of the organism by the substances which it secretes.

There have been observed in man and in horses epidemics and epizooties of tetanus, which are explained by the transportation of the germs through badly disinfected instruments.

The second anaërobic microbe was discovered by Pasteur, who described it, in 1885, under the name of *septic vibrio*. This quite improper designation has give rise to an error which has found expression in certain didactic articles. It has been stated that this microbe is the cause of septicæmias, in opposition to staphylococcus, which is generally believed to be the causative agent in pyæmias. The designation of this microbe as the bacillus of gangrenous septicæmia, a term adopted by the school of Lyons, is not any better. The name bacillus of malignant œdema, used in Germany, can not be accepted, for in France one of the clinical forms of anthrax is thus designated. It is therefore better to abandon all these terms and to adopt the name BACILLUS OF GASEOUS GANGRENE, which has the advantage of avoiding all confusion and of immediately recalling the nature and appearance of the lesions.

This bacillus presents itself at times under the form of small motile rods, isolated or in couplets, measuring from 3 to 5 microns and often including a terminal or median spore; at other times under the form of filaments measuring from 15 to 40 microns and never containing any spores.

Sown on agar-agar, the bacillus of gaseous gangrene produces a cloudy colony with arborization; it liquefies gelatine and blood serum by evolving gas; bouillon is at first turbid, but subsequently becomes clear and full of gas bubbles.

Like the tetanus bacillus, with which it is frequently associated, the bacillus of gaseous gangrene is very widely distributed. It is almost constantly present in the soil, in dung, in the mud of waters; and it is often met with in the alimentary canal of man and animals.

It is a very resistant microbe. Introduced into a wound, it produces a large focus of gangrene with evolution of gas which infiltrates the surrounding tissue. The lesion manifests a great tendency to extension, and death supervenes through intoxication. This microbe, like that of tetanus, remains localized at the point of introduction, and acts through the medium of the toxines which it produces.

Very closely related to, if not identical with, this bacillus is the bacillus of *symptomatic anthrax*. The morphological characters and the appearance of the cultures are similar. The differences lie in their pathogenic action. This microbe attacks cattle, in which it produces a disease called symptomatic or emphysematous or bacterial anthrax. It is of no importance in human pathology, but has acquired great interest because of the numerous researches in general pathology for which it has served. It may not be useless to add that there exists no relation whatever between symptomatic anthrax and the ordinary or bacterial anthrax.

We have yet to mention among the anaërobics the bacillus of Acute Articular Rheumatism. Achalme and Thiroloix have found in the blood of rheumatic patients an anaërobic bacillus which, by its morphological characteristics, is allied to the anthrax bacterium. Triboulet and Coyon have also found a bacillus, but differing from the preceding. These observations are too recent to permit an opinion as to the part played by these microbes.

Spirilla.—Two *spirilla* must be studied. The first known is the Spirillum of Recurrent Fever, discovered by Obermeier in 1873. It presents itself under the form of very motile elements, having 15 to 20 spiral turns and measuring from 15 to 50 microns. It is seen during the paroxysms in the blood of the patient, or of the monkey experimentally inoculated. This parasite has not yet been successfully cultivated.

The microbe of CHOLERA, called also *spirillum of cholera, cholera vibrio,* and *comma bacillus,* was isolated and cultivated by Koch in 1884. It occurs in the form of a half parenthesis, of an S, or of the Greek character ω; at times, however, certain individuals are recti-lineal or drawn out into filaments. In old cultures spherical involu-tion forms are found. This microbe is motile, owing to the presence of numerous cilia.

It develops readily in various culture media; in gelatine it pro-duces small colonies; inoculated by stab culture in a tube, it pro-duces a spherical excavation terminating in a rectilineal prolonga-tion. This appearance is almost characteristic. The microbe liquefies coagulated serum with equal rapidity. Upon agar-agar it forms a white and thick layer; on potatoes, a brown layer. Bouillon becomes turbid and covered with a thin pellicle. Milk does not coagulate.

The development is very readily effected in peptonized water. This medium, which is often employed for its bacterial diagnosis, is charged with a great quantity of indol; treated with nitric acid, the liquid of the culture assumes a violet-red colour. This is the reaction called " *Cholera-roth.*"

The cholera bacillus lives as a saprophyte in water, and as a para-site in the alimentary canal of healthy human individuals. When it becomes excited, it multiplies within the intestinal cavity, which it manifests no tendency to leave; the lesions which it provokes must be attributed to the absorption of toxines to which it gives rise.

Phycomyces.—Close to those bacteria capable of producing infec-tious diseases is reserved an important place for the parasites of a higher order.

The latter are headed by a group of streptothrix, also called *Oospora* or *Nocardia.* The most important of this kind is the *Strepto-thrix bovis* or *actinomyces,* which produces in man and in animals a dis-ease described under the name ACTINOMYCOSIS. Observed in the bovine species by Rivolta (1868 and 1875), who looked upon them simply as crystals, actinomycetes have been better studied by Perroncito, Bol-linger, and particularly by Harz and Israel, who proposed the term now adopted to recall their vegetable nature and their radiate form ἀκτίς), ίνος = rays, μύκης = fungus). The first cases observed in man were published by Israel (1878) and Ponfick (1879–1882).

Actinomyces gives rise to two kinds of lesions: to productions of sarcomatous appearance and to suppurative foci. In both cases yel-low granules have been found, resembling sulphur flowers. The para-site is readily seen on microscopical examination of one of the gran-ules. It is essentially formed in the following manner: a central part, made up of a felting of mycelial filaments, which irradiate like

the spokes of a wheel and terminate in swellings of a club-shaped form or elongated in a *pyriform manner*.

This vegetable, a facultative anaërobic, may be cultivated, although with difficulty, in various media, such as solidified serum, glycerine agar-agar, milk, bouillon, and vegetable infusions.

It lives as a saprophyte upon vegetables, and especially upon the graminaceæ. The herbivora are infected by grazing on the plants. The disease is particularly frequent in cattle, but it is also observed in swine, sheep, dogs, and the horse, although in the latter animal a somewhat different fungus is generally found, known under the name *Botryomyces*. Man is at times infected from the bovine species, exceptionally by a human subject, nearly always through the grain which he has chewed or with which he has been pricked.

The studies of recent years have had a tendency to divide the history of actinomycosis, or at least to admit the action of a whole series of analogous but not identical parasites. Poncet and Dor have cited facts of this kind. Vincent has shown that the disease designated by the name of *pied de Madura*, Madura foot, particularly frequent in India, Algeria, and America, is due to an analogous vegetable parasite, *Streptothrix Maduræ*.

Among the principal pathogenic streptothrices we shall simply mention *Streptothrix asteroides* (Eppinger), which has been quite frequently observed in abscesses of the brain, of the meninges, and of the kidneys; *Streptothrix Foersteri*, found in the form of agglomerated filaments in the calcareous concretions of the lachrymal duct; and particularly *Streptothrix farcinosa* (Nocard), which produces in cattle a disease improperly called farcy (glanders), which is not to be confounded with the glanders of the horse or of man.

The Mucor group also contains a few pathogenic species which are of interest. Such is *Mucor corymbifer,* well studied experimentally by Lichtheim, and found in man by Paltauf.

Mycomycetæ. — Mycomycetæ comprise *aspergillus, penicillium,* and *saccharomyces.* The most important among Aspergilli is *Aspergillus fumigatus.* It vegetates as a simple saprophyte on hemp, and induces pulmonary lesions in those subjects who chew the grains for feeding pigeons. A few but exceptional cases of aspergillosis of the kidneys, skin, cornea, nose, and pharynx have been recorded in man. In a pulmonary abscess presenting certain of the characters of actinomycosis, Wheaton found a parasite which he compares with *Aspergillus niger.* This species is not generally considered pathogenic. Observations and experiments nearly always show that it is *Aspergillus fumigatus* or *glaucus* that is concerned.

A widely distributed vegetable, *Penicillium glaucum,* which is gen-

erally a simple parasite, may, however, occasion general infections. The spores injected into the veins of a rabbit give rise to the development of a pseudo-tuberculosis.

Recent studies have drawn attention to the pathogenic rôle of BLASTOMYCETÆ. We have long known the action of one of them, *Oidium albicans* or *Saccharomyces albicans*. This parasite produces upon the mucous membrane of the mouth a lesion described under the name of aphthæ or thrush. It is a local affection. However, in certain cases, oidium invades the organism, and in man produces a true general infection. At the autopsy, oidium nodules are found in the brain, kidneys, and lungs. Similar results have been obtained in animals, and these findings have thrown considerable light upon the mechanism of nonbacterial infections.

The interest of blastomycetæ is increased by recently published researches which establish the fact that these fungi are encountered in man much more frequently than was formerly believed. It will be seen in another chapter what an important rôle is attributed to them in the genesis of tumours.

Protozoa.—Along with vegetable microbes are to be classed the animal microbes. We must place in this group the rhizopods and sporozoa, which alone are of importance in human pathology.

Among the RHIZOPODS we shall mention *amœbœ*, which have been met with in the tartar of the teeth, in gingival abscesses, and in the vagina. Their importance has increased since the studies of Loesch, and particularly of Kartulis, have shown their presence in the intestines of dysenteric patients. Is it to be concluded that the *Amœba coli* is the cause of dysentery, and that it is also capable of producing the hepatic abscess consecutive thereto? This question is not yet solved, although an answer in the affirmative is quite probable.

The SPOROZOA are divided into the gregarinæ and psorospermiæ.

The gregarinæ represent parasites which are mostly found in invertebrates. Of late they have been observed in mammalia. Pfeiffer says he has found them in man in cases of smallpox, in vaccinia, scarlet fever, and herpes zoster; but their pathogenic function is by no means established.

Psorospermiæ possess much greater interest. With this group are classed the *coccidia*,* which were first studied in animals. They are

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* Besides the coccidia, psorospermiæ include:

(1) Myxosporidia, which are encountered in fish and which we have observed in the liver of a mouse.

(2) Sarcosporidia (Miescher's tubes, Rainey's tubes), which invade the muscles of various mammalia. Rosenbergen found them in the myocardium of a woman forty years old.

(3) Microsporidia, which inhabit worms and insects, and produce in silkworms the disease designated by the name of *pebrine*.

frequently met with in the liver of rabbits, where they invade the biliary passages and give rise to epithelial and connective-tissue proliferations. Observed several times in the intestine, liver, kidneys, and pleura of man, coccidia are at present often looked upon as the cause of cancer. This conclusion, to which we shall again refer when speaking of tumours, is supported only by histological proofs. No one has as yet succeeded in cultivating the parasites, still less in inoculating them. Lively discussions have therefore arisen on the subject, many scientists considering that the forms described as coccidia represent simply degenerated cells.

It is with a group allied to the coccidia that most naturalists class the parasite of malaria, Laveran's *hematozoon, Plasmodium malariæ*; *Laverania malariæ*, as it is justly called in foreign countries. Although it has not been possible to isolate and cultivate the parasite, observations are now so numerous that there can no longer be any doubt as to its etiological significance. The element discovered by Laveran certainly is the causative agent of malaria. It lives within the red blood corpuscles and presents itself under the various forms of spherical bodies, spherical flagellated bodies, and also of crescents and rosettes.

Summary and Classification of the Infectious Agents.—If we consider the results which have been obtained by the study of pathogenic agents in infectious diseases, we may conclude that wonderful discoveries have been made. To-day nearly all diseases have their microbe. Those diseases in which the pathogenic agent is as yet unknown are not numerous, but, curiously enough, they belong to that class the infectious nature of which is not a matter of much doubt, and whose contagion is best established—e. g., the eruptive fevers, measles, scarlet fever, smallpox, varicella, vaccinia, the clearly infectious skin diseases like herpes zoster and polymorphous erythema, and those diseases which are never transmitted otherwise than by direct contact—rabies and syphilis.

A. Nonspecific Bacteria.

Micrococci.

Staphylococcus.
Aureus.
Citreus.
Albus.
Streptococcus.
Pneumococcus.
Tetragenus.

Bacilli.

Colon bacillus.
    Paracolon bacillus.
        Bacillus of psittacosis.
        Pneumobacillus.
    Bacillus septicus putidus.
    Bacillus of hemorrhagic septicæmia.
    Proteus vulgaris.
    Bacillus pyocyaneus.
    Leptothrix buccalis.

SPECIFIC BACTERIA.

Micrococci.

Gonococcus.
Micrococcus of mumps.

Bacilli.

Bacillus anthracis.
Bacillus of glanders.
Bacillus of typhoid.
Bacillus of diphtheria.
Bacillus of influenza.
Bacillus of tuberculosis.
    Bacillus of human tuberculosis.
    Bacillus of avian tuberculosis.
    Bacillus of fish tuberculosis.
Bacillus of leprosy.
Bacillus of bubonic plague.
Bacillus of yellow fever.
Bacillus of soft chancre.
Bacillus of tetanus.
Bacillus of gaseous gangrene.
    Bacillus of symptomatic anthrax.
Bacillus of rheumatism.
Spirillum of recurrent fever.
Bacillus of cholera.

B. PHYCOMYCETÆ.

Streptothrix.

Streptothrix bovis (actinomyces).
Streptothrix Maduræ, asteroides, Foersteri.
Streptothrix farcinosa.

Mucor.

Mucor corymbifer.

C. MYCOMYCETÆ.

Aspergillus.

Aspergillus fumigatus.
Aspergillus glaucus.

Penicillium.

Pencillium glaucum.

Saccharomyces.

Saccharomyces or Oidium albicans.

D. PROTOZOA.

Rhizopoda.

Amœba coli.

Sporozoa.

Coccidia.
Hematozoa.
Plasmodium malariæ.

CHAPTER VII

ANIMATE AGENTS (Concluded)

Distribution of microbes in water, soil, and air—Resistance of microbes to external agents—Antiseptics—Distribution of microbes in living beings—Rôle of microbes normally inhabiting the organism—The microbes of the alimentary canal—Gastrointestinal fermentations and putrefactions.

Distribution of Microbes

Water, as is well known, contains a great number of microbes; rain, snowflakes, and hailstones collect some of them in the atmosphere. There is no pure water except spring water at its source. Water containing from 50 to 160 bacteria per cubic centimetre is considered an excellent drinking water. These figures are much exceeded in the majority of rivers, especially when they have passed through a city; these water courses, however, possess the property of spontaneously purifying themselves. A very simple observation proves this: it suffices to examine the Seine below the collector of Asnières; the water, overcharged with organic matters, is brownish, of a disagreeable odour, and at every moment gas bubbles burst on its surface, evidencing the intensity of fermentations going on. A few kilometres farther down the water again becomes limpid.

The following figures offer examples in this regard: The Isar, before passing through Munich, contains 305 bacteria per cubic centimetre; at its issue from the city, when it has received the products of sewers, it contains 12,600; 13 kilometres farther down, without having received any tributary, the figures fall to 2,400 per cubic centimetre.

Natural depuration is produced equally in reservoirs. The water of the Thames, for example, contains 1,437 bacteria. It contains only 318 after its passage into a first reservoir and 177 at its issue from a second.

In rivers the agitation of the waters causes the microbes to unite with solid particles, and thus some are destroyed. If we take water containing 155 bacteria and agitate it with some chalk added in the

proportion of one fifth, there will remain only 10; with charcoal powder, the quantity falls from 8,000 to 60; with pulverized chalk, the results are still more striking—the water is sterilized, even when the number of microbes was so great that it was impossible to count them.

More important is the action of the sun, the rays of which exert an inhibitory influence on bacteria, as has been proved by a great number of experimenters. Pansini introduced a few drops of a culture of asporogenic anthrax into water which he submitted to the action of the sun; then the number of bacteria per cubic centimetre was 2,520; at the end of twenty minutes it fell to 130; at the end of half an hour, to 44; after forty-five minutes there were none found.

The results are identical with other microbes. Procaccini took sewer water containing from 300,000 to 420,000 bacteria per cubic centimetre and submitted it to the action of the sun. At the end of the day the liquid was sterile.

Here is another experiment, which realizes the conditions perfectly. The water of the Isar, before its passage to Munich, was studied by Buchner at different hours of the same day. The highest figure was found at 4 A. M.; bacteria had multiplied during the night and their number reached 520 per cubic centimetre. The minimum was obtained at 8 P. M.; sunned all day, the water did not contain more than five bacteria per cubic centimetre.

Among the pathogenic microbes most frequently encountered in water, we must mention the colon bacillus, typhoid bacillus, staphylococcus, streptococcus, the bacillus of gaseous gangrene, and, in certain cases, the anthrax bacterium, the vibrio of cholera, etc. Once in water, microbes can not come out of it; consequently, they can not get access to our organism except through ingestion. When the level sinks, they are deposited upon the uncovered soil and are then easily disseminated. Pettenkoffer has made an application of this result to his celebrated theory on the variations in the level of subterranean waters. According to him, when the level sinks, typhoid fever increases; when it rises, it decreases. Unfortunately, many exceptions have been recorded; in some cases the variations of typhoid fever have occurred just in the contrary order.

The *soil* contains a great number of bacteria, some of which are indispensable to vegetation. The works of Schloesing, Muntz, and Winogradsky have established their intervention in nitrification. For us, as we are considering the pathogenic phenomena, it suffices to know that pathogenic microbes are found in the soil: the bacilli of tetanus and of gaseous gangrene, the microbes of suppuration, and in certain cases the bacilli of typhoid fever, of tuberculosis, of anthrax, and of cholera. To this list should be added the saprophyte agents, which,

although inoffensive of themselves, may, when they enter our tissues, favour the development of pathogenic agents.

It is easy to understand that in most cases the soil is contaminated with products emanating from diseased men and animals; that it is not more infected, is due to the germicidal action of the sun's rays, which rapidly destroy the microbes remaining on the surface; but they act with less energy upon those which have sunk into a certain depth. One might believe that the latter are no longer capable of harm; unfortunately, this is not so, for they may, under certain conditions, be brought up to the surface. This is what was brought out by the celebrated researches pursued by Pasteur on the etiology of anthrax in the infected districts of Beauce, then designated under the name "cursed fields." It is to be noted first that animals or their cadavers affected by anthrax never contain spores; the bacteria would then be speedily destroyed, if blood or liquids containing them were not spread on the external mucous membranes and integuments and did not at the same time fall on the soil. Once out of the organism, bacilli rapidly give birth to spores, some of which contaminate the soil; others, developing on the cadavers, are buried with them. Then, according to a theory, arrive the earthworms, which ingest the spores, raise them to the surface, and, depositing them in their excretions, spread them upon the surface of the soil. They may afterward be transported and disseminated far off by wandering animals like the slugs, which in one day travel a great deal (Karlinski); or they may be swallowed by insects, some of which, provided with a sting, act as agents to inoculate man.

Being thus spread upon the surface, the spores contaminate the vegetable growth; so herbivorous animals are infected by eating the plants. The infection takes place in the mouth when the mucous membrane is scratched by the spikes, or in the intestine.

The researches which have been made with the typhoid bacillus have established that this microbe is quickly destroyed on the surface of the soil. It does not resist the action of the sun, but at 50 centimetres of depth it finds excellent conditions of resistance and may retain its vitality for over five months.

The number of microbes diminishes in proportion to the depth below the surface; the maximum is at 50 centimetres, and below 3.5 or 4 metres there are none to be found.

There remains a last question. Can the microbes of the soil invade vegetables? They can, according to Dr. Galippe. He has recorded a great number of experiments which have raised lively controversies. The problem is not yet solved; but, in view of its great practical interest, it deserves to be studied anew.

The dust of apartments, tapestry, woodwork, and floors contain numerous pathogenic microbes. In hospital wards, in cases of epidemics, there have been found between the planks of the floor the microbes of tetanus, erysipelas, pneumonia, and diphtheria. The same is true as regards tuberculosis; every author cites the researches of Cornet, who, in a room occupied by a consumptive, found that the dust obtained by scratching the wall, when inoculated into the peritoneum of a guinea pig, induced tuberculosis.

The *air* serves much less to transmit infections than the soil, and still less than the water. It contains, however, a great number of microbes, as shown by the following figures, obtained by Dr. Miquel, which at the same time show clearly the considerable variations of the numbers depending upon the place:

In the sea, at 100 kilometres from the coast	0.6
Altitude of 2,000 metres	3
Summit of Pantheon	200
Observatory of Montsouris	480
Rivoli Street (in Paris)	3,480
New house	4,500
The air of sewers of Paris	6,000
Old house	36,000
Hôtel-Dieu (hospital)	40,000
Pitié Hospital	79,000

One may be surprised, in perusing this list, to see that the air of sewers contains but a slightly greater number of microbes than the air of a new house, and six times less than that of an old house. It is because the innumerable bacteria contained in water can not invade the air. It has been experimentally shown that a current of air passing over a contaminated liquid is not charged with microbes. The reverse opinion once prevailed; it was at one time believed that the air served as an intermediary between the water and our organism, and in support of this idea the events of an infectious character consequent on the inhalation of gases escaping from sewers or cesspools were cited. In reality, the mechanism is more complex: the gases act by disturbing the economy and by reducing its resistance; they thus permit the development and exaltation of pathogenic germs which, until then, vegetated as simple, inoffensive parasites.

The various results above recorded have but a relative value; very notable variations occur every day in the same place. During the hot season microbes increase, to reach their highest figure in the month of July; the minimum occurs in December. Their numbers diminish after a rainfall which carries them toward the soil; they diminish

equally under the influence of the sun's rays, the germicidal power of which has already been referred to.

Researches have in most cases been limited to a simple counting of the microbes of the air, regardless of the proportion of pathogenic agents. But clinical observations suffice to inform us in this regard. It is admitted that typhoid fever may be transmitted through the air far more rarely than by water. The same applies to eruptive fevers, but it is to be noted that this mode of propagation is rare and occurs within a restricted zone. The virus of measles hardly extends beyond 4 metres, that of scarlet fever is perhaps a little more diffusible. As to smallpox, the better we study the march of epidemics the more we are convinced that contamination takes place in most cases, if not always, by direct contact.

One of the infections which are transmitted most frequently through air is tuberculosis. The particles of desiccated expectoration are swept by the wind and penetrate the respiratory channels, and this accounts for the frequency of pulmonary lesions.

The air has often been supposed to play a part in the transmission of surgical infections; it is to-day demonstrated that erysipelas, septicæmia, and gangrene are generally propagated, not through the air, but by the hands of the surgeon and his assistants, by the instruments and dressing material. The same is true of puerperal fever: women attacked with erysipelas may be confined, even in an isolation ward devoted to the treatment of this infection, without becoming septicæmic, provided necessary care and precautions be taken.

One of the infections most frequently propagated by the air is malaria. The hematozoon may be transported to great distances from the marshes where it led its saprophytic life; but an obstacle of land, a wall, a cluster of trees suffices to arrest its passage.

RESISTANCE OF MICROBES

Microbes are submitted to a certain number of destructive causes, which may, according to their intensity, produce three different effects: functional modifications, a diminution in numbers, or a complete destruction. It is because the cultures are not homogeneous that the number can decrease; if all the individuals possessed the same vitality, all would perish at the same time.

The resistance of microbes varies, on the other hand, according as the cultures do or do not contain spores: if they do not, resistance is, as is known, much less marked.

The agents capable of doing harm to bacteria are also divisible into four groups: Mechanical, physical, chemical, and animate agents.

Contrary to what has often been asserted, *mechanical agents* pos-

sess but little action. We can not admit, for example, that the varia-
tions of atmospheric *pressure* can modify the activity of the patho-
genic bacteria, increase or diminish their virulence, and thus explain
the epidemic temperament (*génie épidémique*). The contrary opinion
finds its origin in the erroneous interpretation of exact experiments.
It has been shown, in fact, that certain compressed gases exert a
noxious action on microbes; but in this case the effect is not simply
due to an increase of pressure; the phenomena are much more com-
plex.

If, for example, we make the oxygen act under a pressure of 10
atmospheres, we may kill the *Bacillus anthracis*; still, it is necessary
to prolong the contact for a very long time. When the microbe is not
a spore-bearing one, less than eight days will not suffice; when it
does bear spores, death does not occur even at the end of twenty-
one days.

Carbonic acid appears to be more energetic. According to
Fraenkel, Seltzer water is sterilized in the siphons. D'Arsonval has
seen a certain number of bacteria perish under a pressure of 60 atmos-
pheres.

From all these researches it may be concluded that oxygen and car-
bonic acid can kill microbes, provided the pressure be considerable.

To make evident the true action of pressure, we have inclosed vari-
ous microbes in rubber tubes which have been plunged in water or in oil.
By compressing the liquid to 2,000 kilogrammes per square centi-
metre, we observed no modification of the four species employed:
streptococcus, staphylococcus, colon bacillus, non-spore-bearing and
spore-bearing anthrax.

Going up to the strongest pressures which one could reach—that is,
to 3,000 kilogrammes (2,903 atmospheres)—we obtained the follow-
ing results: Colon bacillus and *Staphylococcus aureus* have experi-
enced no disturbance; the non-spore-bearing anthrax, sown in a fresh
medium, developed more slowly than it habitually does, and proved
less virulent than before compression; the spore-bearing anthrax was
slightly attenuated; streptococcus vegetated less luxuriantly, less rap-
idly, and furthermore lost part of its toxic action. It is necessary,
then, to reach colossal pressures in order to observe some, anyhow
little marked, modifications in the vitality or the properties of bacteria.

It had been thought, after the researches of Horvath, that slight
movements or oscillations of the culture medium prevented the devel-
opment of microbes. Further experiments have not confirmed this
result; the effects have been variable and inconstant. For our part, we
have obtained no results by submitting cultures to repeated shocks
reaching 200 to 250 kilogrammes per square centimetre.

Physical agents have a far greater importance, at least some of them. Some, for instance *cold,* are very well borne. We have already said that microbes are found in ice. Dr. Raoul Pictet submitted bacteria to temperatures as low as — 110° and even — 200° C. without succeeding in killing them. Professor d'Arsonval plunged some into liquefied air, without causing them to lose their power to vegetate. It is possible, however, to do harm to bacteria even with less low temperatures, by submitting them to successive freezings and thawings; their numbers notably diminish in these conditions.

Heat has a much more marked action. There are undoubtedly certain species, notably those of hot springs, which seek heat and vegetate best at a temperature of 70° and 74° C. This is, however, an exception. Bacteria are easily destroyed by heat, but effects vary according to several conditions, as usually the spores prove much more resistant than the adults. All other conditions being the same as regards the culture, heat is more destructive when microbes are contained in a liquid medium than when they are dried up. Finally, the action of heat is considerably favoured by the presence of air, which produces oxidations unfavourable to bacteria.

The multiplicity of conditions intervening at the same time as heat explain the often considerable differences obtained by experimenters. The figures given have but a relative value; they nevertheless present a certain interest.

Let us take, for example, the tubercle bacillus: plunged into water at 60° C., it is still living at the end of twenty minutes; into water at 70° C., at the end of ten minutes. Boiling water, at 100° C., kills it in five minutes. If dry heat is brought to act, the bacilli resist a temperature of 100° C. for several hours.

The differences are the same for anthrax. According to Dr. Momont, anthrax blood, desiccated in a vacuum, remains virulent after a sojourn of an hour and a half in an oven at 92° C.; the moist blood is sterilized at 55° C. in one hour. To kill the spores, we must submit them, according to Koch and Wolffhügel, to 107° C. for five minutes, when they are moist; if dry, they resist 120° C. for four hours; to make their destruction sure, we must leave them three hours at 140° C. It is true that Massol finds less elevated figures. A temperature of 100° C. kills the spores at the end of five or six minutes.

The influence of air is made apparent from Dr. Roux's experiments. Submitted to the combined action of air and a temperature of 70° C., spores succumb in 60 hours; protected from air, they still live at the end of 165 hours.

We have already shown, with respect to microbes of the soil, the important part played by *light.* The blue and violet rays act most

energetically; but, as in the case of heat, the action of the light is favoured by moisture and by air. Dr. Momont has shown that anthrax spores perish after 48 hours of insolation when they are in contact with air; inclosed in a vacuum, they are still living after 110 hours. The action of light may be evidenced by the following experiment: A few drops of an anthrax culture are spread upon a gelatine plate, which is then covered with a glass upon which pieces of black paper are pasted; on exposure to the light, development takes place in the protected parts and the bacteria exactly reproduce the designs figured by the pieces of paper.

The action of light is more complex; for, besides the noxious influence exercised on bacteria, the modifications of the medium are to be taken into account; sunned bouillon becomes unfit for cultivation.

In cases where life persists, functional modifications supervene: chromogenic microbes cease to produce pigment, and pathogenic agents become attenuated.

We shall not dwell upon the effects of *electricity*. In the old experiments the currents employed produced heat or electrolysis, and the effects obtained were of a thermal or chemical order. Those authors who have been on their guard against these causes of error have not been able to detect a direct action of electricity on microbes.

The *chemical agents* that act upon bacteria are called *antiseptic agents*. Among the gaseous bodies, it suffices to mention ozone, which, as is known, is often found in the air in great quantities. Its action is very intense, at least on the adult elements; the non-spore-bearing anthrax is killed within five hours, but the spores perish only at the end of three or four days.

The antiseptics, properly so called, when used in minute doses, have the very curious property of stimulating the activity of microbes; under their influence, the chromogenic bacteria produce a greater quantity of pigment. In increasing the dose of the antiseptic, we see the chromogenic power diminish and disappear; then vegetation grows slower, ceases, and finally the microbe is killed.

Carbolic acid is one of the substances most frequently employed. In a 1-per-cent solution it kills the non-spore-bearing bacterium in ten seconds; if the element is spore-bearing, life persists after the continued intervention for thirty-seven days of a solution five times stronger.

In order to increase the action of antiseptics, it is well to raise the temperature of the medium; this is an element of capital importance from a practical standpoint. For disinfecting purposes hot solutions must be employed. The anthrax spores, for example, resist 5-per-cent carbolic acid at the surrounding temperature, but they are killed in the

same solution in two hours if the temperature reaches 55° C., and in three minutes if it is raised to 57° C.

By submitting a microbe to the influence of antiseptics during several successive generations, we can permanently modify it and deprive it of some of its properties. Thus are created non-pigment-forming, non-spore-bearing varieties, and, what is more important, the virulence is made to disappear and vaccines are obtained.

The action of *animate agents* upon bacteria now remains to be considered. In a great number of cases, two or more microbes vegetate in the same medium. Sometimes they assist each other; thus, for example, an aërobic microbe, by appropriating to itself the oxygen, will facilitate the development of an anaërobic. More frequently they antagonize each other; in cultures originally polymicrobic one species will little by little predominate and finally stifle the others; a natural selection is effected. Moreover, microbes have frequently to struggle with the higher organisms, vegetable and animal, whether they occupy their integuments or penetrate into their interior. We are thus led to study the behaviour of bacteria toward higher beings.

Distribution of Bacteria in Living Organisms

The distribution of microbes in the air, soil, and water suffices to explain their presence on all the exposed parts of our bodies. They are found in great number upon the *skin*; they live there as inoffensive parasites; the horny epidermis, further protected by a layer of fat, opposes to them an impassable barrier.

With each inspiration, the air causes a great number of bacteria to penetrate the *respiratory passages*. They are retained by the hair in the nasal orifices and by the vibratile cilia of the mucous membrane. Others are fixed by secretions; they become pasted, as it were, to the moist tissues. Therefore the farther we recede from the natural orifices the smaller the number of bacteria do we find. At the level of the pulmonary alveoli, often at the level of the bronchi or even of the trachea, the air is bacteriologically pure. In again passing through the respiratory tract, at the moment of expiration, the air does not take up the parasites which it has deposited, for, as we have already said, these can never leave the liquid media which encompass them. The expired air, therefore, contains no microbes.

It may be inquired: What is the fate of the bacteria that are thus deposited and that might become harmful, if only by their number? Fortunately, the respiratory apparatus is provided with various means of protection. The secretions act mechanically and wash, so to say, the mucous membrane; a certain number of bacteria are thus thrown out. Others are destroyed by the nasal mucus, which, as has been

shown by Lermoyez and Wurtz, possesses germicidal powers.   In other
words, the secretions exercise a sort of antiseptic action.   The re-
mainder are picked up and devoured by certain cells called phagocytes,
which are very numerous in those localities where lymphoid tissue
abounds, and at the level of the pulmonary alveoli.

Bacteria are much more numerous in the *digestive canal*.   Ingested
with the food and beverages, they reach the stomach, where, according
to certain authors, the acid has the property of destroying them.   This
assertion, based upon results obtained by means of artificial digestion,
explains the frequency of infection when the subject is fasting, when
the stomach is altered, or the gastric juice is neutralized by an alkali.
It seems, however, that the protective rôle of the stomach has been
somewhat exaggerated; for counts which have of late been made show
that this portion of the digestive tract contains numerous bacteria,
even more than the duodenum.

Having reached the intestine, the microbes here find the best con-
ditions for their existence.   The aliments we ingest serve for their
nutrition; the heat of our digestive tract offers them the advantages
of a well-regulated oven; the secretions which flow are far from being
germicidal, since they contain substances favourable to their develop-
ment.   We may therefore say that the alimentary canal is the paradise
of microbes, and that they can multiply energetically, as is shown by
the following figures, taken from the interesting researches of Gilbert
and Dominici.   There are found in the stomach 50,000 microbes per
cubic millimetre; then the figure suddenly falls; at the origin of the
duodenum there are only 30,000; the number progressively rises until
the end of the bowel is reached, where it attains its highest point—
namely, 100,000 per cubic millimetre.   In the cæcum another fall
occurs; throughout the length of the large intestine there are only
25,000 to 30,000 microbes per cubic millimetre.   By taking account of
the quantity of matter contained in the digestive canal, we arrive at
the respectable total of 411,000,000,000 microbes.

Each day man rejects a certain number of bacteria in his fæces.
In health the quantity varies from 12,000,000,000 (Gilbert and Domi-
nici) to 40,000,000,000 (Vignal).

According to some authors, these microbes play a salutary part;
they perform a second digestion, complementary to that accomplished
by the digestive juices.   This idea, developed by Dr. Duclaux, has led
to the supposition that perhaps life would be impossible without the
aid of these collaborators, which are to animals what the microbes of
nitrification are to plants.   The hypothesis is seductive, and it is
doubtless very interesting to study what would become of animal life
without the intervention of bacteria.   An experiment, difficult to real-

ize, has, however, been conducted by Nuttal and Thierfelder. By means of a very ingenious contrivance these authors succeeded in breeding two guinea pigs protected from microbes. Unfortunately, the experiment lasted but eight days; during this time, however, these animals flourished just as well as the control animals left in the free air. It is evidently impossible to conclude what would happen later. These researches are worthy of repetition.

Whatever be the solution employed, it is incontestable that microbes cause our aliments to undergo profound transformations, some of which are similar to those of digestion, others differing therefrom in that the modification of substances is greater.

The albumens are peptonized, but at the same time there are produced amido agents, leucine, tyrosine, and particularly aromatic bodies, indol, phenol, and skatol. The last-named, slightly soluble, remains almost entirely in the fæces and gives to them their peculiar odour. Indol and phenol are reabsorbed, and, after certain modifications within the organism, are eliminated in the urine. Coincidently, there are produced volatile substances, carbonic acid, ammonia, sulphuretted hydrogen, methylmercaptan (a substance with a nauseous smell, entering into ebullition at 21° C.), of which one part is expelled by the anus, and another, being reabsorbed, is eliminated by the respiratory apparatus and the skin. Finally, there are formed ptomaines, which, from their chemical constitution, are analogous to vegetable alkaloids. With a view of recalling their origin and their toxic effects, the principal ones have been denominated ptomatoatropine and ptomatomuscarine. It is then easily understood that fæcal matters are toxic. According to Bouchard, the extract of 17 grammes suffices to kill 1 kilogramme of animal.

The action on the other groups of aliments is less important from a pathological standpoint. The carbohydrates are transformed into alcohol—and this explains the presence of this substance in the organism of animals—and into acids. The cellulose is attacked and the fats are broken up.

Certain aliments, like milk, hinder fermentation; others favour it. Bouillon, meat, particularly veal, offer excellent culture media for bacteria. Putrefactions reach their highest intensity when tainted alimentary substances are ingested. The use of venison, or of dishes made with ill-preserved cold meat, may often produce grave disturbances. These are particularly frequent in Germany, where they are described under the name botulism or allantiasis. They result from the ingestion of very large sausages, the central portions of which are incompletely cooked. This element contains perfectly formed ptomaines as well as microbes. Ptomaines chiefly serve to diminish the

resistance of the organism; they favour the multiplication of microbes, and, after an incubation period of from twelve to fifteen hours, disturbances make their appearance. These are manifested by vomiting, a horribly fetid diarrhœa, and, in the grave forms, cutaneous eruptions, nervous manifestations, dizziness, and diplopia. Lastly, in certain cases, the temperature falls, the extremities grow cold, and the patient succumbs in collapse.

Poisonings have been occasioned by the use of preserves. The central parts of the boxes are not always sufficiently heated and may contain dangerous microbes.

Preserved fish, and particularly preserved lobster, have thus caused serious disturbances. The same is true of salted codfish; its dangerous character is indicated by the rosy colour which it presents and which is due to a fungus—viz., *Beggiatoa roseo-perniciosa*—which is not dangerous by itself, but is accompanied by putrefactive bacteria.

Milk may also be altered; it contains a poison studied by Vaughan —tyrotoxine—which produces serious disturbances, notably in children.

The intestinal putrefactions, when exaggerated by some cause or another, occasion a whole series of disturbances. Locally, an irritation of the bowel is produced, which is expressed by expulsive colics and diarrhœa, and nauseous evacuations. Part of the volatile principles is absorbed and is eliminated by the breath and by the sweat, which takes on a fetid odour; there are present at the same time lassitude, dizziness, and headache—all phenomena denoting intoxication of the organism.

Reciprocally, in case of constipation, the intestinal products are reabsorbed; the manifestations are similar, but less marked, for the fæcal matters are harder and absorption is less easily effected; the symptoms are again dizziness, headache, fatigue, and fetid breath and sweat.

Generally these disorders are not of serious import in normal individuals; but not so with certain patients, notably those having recently undergone an operation, and, above all, with puerperal women. A febrile state is observed, at times disquieting, which yields to the influence of an enema, a purgative, or an antiseptic.

In still severer cases there occurs intestinal obstruction, in which, among numerous disturbances, several are referable to the reabsorption of toxines.

When the stomach is profoundly affected, and notably in dilatation of this organ, the exaggeration of putrefaction gives rise to a series of morbid manifestations. On awakening, the patient feels more tired than at bedtime. He suffers from headache and dizziness; the passage

of toxines through the kidneys induces albuminuria; their action on the bones produces various alterations, such as nodes at the level of the second phalanx, and osteoporosis. In childhood rickets is the consequence of disturbances of intestinal digestion which are so frequent at that age.

Two still graver symptoms may depend upon exaggerated gastric fermentation: tetany, which is sometimes fatal, and diacetæmic coma, which we shall study more fully in connection with diabetes.

It is easy to understand that in a great number of general diseases, markedly in infections, intestinal putrefactions increase by reason of the fact that the means we possess for preventing them decrease.

The digestive canal can expel microbes by the same procedures as other parts of the organism; the intestinal and pancreatic juices and the bile, although not possessing any antiseptic property, act as cleansing agents and at once reject microbes and toxines. If bacilli tend to pass through the mucous membrane, they are arrested by the lymphoid organs—solitary glands and Peyer's patches—and by numerous leucocytes, which constantly travel in these regions, and can even make their way into the cavity of the intestine.

If they escape these causes of destruction, microbes reach the lymphatic glands and the liver, where new means of defence are found. If they pass beyond, they reach the lungs, which are also endowed with germicidal power. We thus see how many precautions are accumulated against the microbes of the bowels.

Protection against microbic toxines is assured by the digestive secretions, which transform some of them, throw out others, and particularly by a very special action of the intestinal mucous membrane. Taking up an idea of Stich, Denys and Brion have proved that the epithelial cells of the intestine destroy the microbic toxines; those that escape pass through the liver, which neutralizes some of them. But the protective function of this gland is quite variable. It is very pronounced with the toxines of certain varieties of the colon bacillus, but does not seem to be exercised upon poisons produced by other species. So, in many cases, the poisons pass onward, and are eliminated by the kidneys. Thus the toxicity of the urine chiefly depends upon intestinal putrefaction; it varies parallel to this.

There yet remain the volatile substances, sulphuretted hydrogen and methylmercaptan, which are eliminated by the lungs and the skin, imparting a foul odour to the breath and the sweat. It is to be noted that the liver intervenes here with great energy; numerous experiments prove that it retains and neutralizes considerable quantities of sulphuretted hydrogen.

Intestinal fermentation may be overcome by dietetics and by therapeutics.

It suffices to confine one's self to a milk diet in order to restrict putrefaction in the bowels. Gilbert and Dominici found in the fæcal matters of a normal man 67,000 bacteria per cubic millimetre; after two days of milk diet, there were no more than 14,000; at the end of three days, 8,000, and of five, 2,250. Sterilized milk, by the way, gives no better results; at the end of ten days the stools contain 3,000 bacteria per cubic millimetre.

These differences, already very notable, appear still more marked when account is taken of the quantity of matters discharged. Placed upon a mixed diet, a man passes 175 grammes of fæces, containing 12,000,000,000 bacteria; under the influence of milk diet, the quantity falls to 73 grammes containing only 164,250,000 bacteria—that is, $\frac{1}{71}$ of the original figure.

Of the procedures furnished by therapeutics, we must first mention purgatives, the influence of which has been demonstrated by numerous experiments; one may employ saline purgatives, which expel the microbes, as well as calomel, which has the advantage of possessing a notable antiseptic action.

To inhibit the development of microbes, one may resort to insoluble antiseptics which traverse the digestive canal without being absorbed: naphthol, benzonaphthol, and betol are the substances generally used. In order to prolong their action, it would be well to prescribe them in fractional doses. Benzonaphthol and betol are less active than naphthol, but they do not possess the acrid and burning taste of the latter. So they may be used in the cases of children.

To these substances is often added subnitrate or salicylate of bismuth. The subnitrate renders the stools thicker and exerts a chemical action. In contact with sulphuretted hydrogen, it is decomposed and gives rise to sulphide of bismuth, an insoluble body that neutralizes the harmful action of sulphuretted hydrogen. Salicylate of bismuth does not act quite as well, but it has the advantage of furnishing information concerning the intestinal putrefactions. The salt is decomposed and the salicylic acid resulting therefrom passes into the urine, where it is easily detected by the addition of perchloride of iron, which yields a beautiful violet colour. This reaction does not occur when the production of sulphuretted hydrogen has ceased.

CHAPTER VIII

GENERAL ETIOLOGY OF INFECTIONS

Hetero- and auto-infections—Morbid contagion and spontaneity—Causes favouring infection: immunity and predisposition—Microbic associations—Modes of entrance of microbes—Modes of protection of the organism—Local lesion—Part played by lymphoid productions—Protective part played by certain organs—Importance of the liver and the lungs—Causes explaining microbic localizations: mode of entrance; physiological and pathological state of the organs.

INFECTIOUS diseases may be produced in two ways: they may result either from the introduction into our organism of virulent germs coming from without, or they may be due to microbes that have their lodging within our bodies, and which become exalted under the influence of various intercurrent causes. Infections may therefore be divided into two groups: *Hetero-infections,* recognising an external origin, and *auto-infections,* of which we carry the germs in ourselves, even under normal conditions.

This division, which may be retained, has not an absolute value. It is evident that all microbes that live in us come from outside. But once introduced into our organism, they behave differently. Some remain in the condition of harmless parasites until the time when a morbific cause, diminishing our resistance, enables them to induce a disease. Others act immediately, and their introduction is soon followed by the appearance of morbid manifestations. Yet others hold a position intermediary between the two preceding groups. When they reach us, instead of remaining altogether inoffensive, they provoke a slight, circumscribed lesion, which is sometimes latent and often curable. While the pathogenic agent remains thus localized, even when nothing reveals its presence, the organism is always threatened by accidents; on the slightest occasion the microbe becomes again aggressive and the local lesion is made the starting point of a more or less serious infection.

Let us take some examples. Among the pathogenic microbes that may live for a very long time without occasioning any disorder, we find

staphylococcus, streptococcus, pneumococcus, and colon bacillus. Of microbes producing infection soon after they penetrate an organism, we may cite the agents of anthrax, hydrophobia, syphilis, and soft chancre. In the last group is placed the tubercle bacillus, which may for years locate itself in a ganglion without giving rise to any notable result.

It is further to be noted that the same infection may be brought about in several different ways. Pneumonia, for instance, is due to pneumococcus, which vegetates in the mouth as a harmless parasite; let some accessory cause decrease the resistance of the organism, the microbe will invade the lung and provoke pneumonia. From this moment the exalted germ is able to attack other persons; in this manner the disease born by auto-infection spreads by hetero-infection.

Pathogenic microbes may be introduced in several different ways. There is, in the first place, *direct inoculation*. A virulent microbe comes to soil the surface of a wound, or penetrated with an instrument into the tissues. All wounds are not equally apt to be invaded by bacteria. Those clean cut are seldom infected; not that microbes are lacking on their surface, but they do not find conditions favourable for their development. Contused wounds represent, on the other hand, an excellent medium of culture; the tissues being affected in their vitality, the cells are unable to prevent the multiplication of morbid agents.

The microbes of suppuration, gangrene, and tetanus develop rather in the contused wounds. For other more virulent agents the slightest abrasion suffices for infecting the economy; such is the case with anthrax, glanders, hydrophobia, syphilis, and soft chancre. Against these viruses our resistance is very weak, and inoculation is too frequently positive. There are, nevertheless, some very curious examples of immunity. Certain individuals do not contract venereal diseases, although they do not fail to expose themselves to contagion; others prove rebellious to vaccine, and, in this case, clinical observation has the value of a laboratory experiment.

The second mode of transmission of disease is represented by *contagion*. The microbe does not break in, but penetrates through the natural channels.

Contamination may occur in different ways. In some cases there is contact of the healthy subject with the sick. In other instances the transmission is indirect; it takes place through the atmosphere, objects, or persons who carry the microbe without being themselves contaminated.

Immediate contagion is a matter of evidence; but transportation by air is more conjectural. The latter has been imagined to explain the course of epidemics; as regards influenza particularly, it has been

said that atmospheric transmission made it possible for this disease to pass in twenty-four hours from Berlin to Paris. In analyzing the facts, however, we perceive that epidemics do not go any quicker than our means of communication; they are propagated, not by the wind, but by direct contagion.

Individuals who have taken care of patients, or simply approached them, may transport the disease. Certain epidemics of puerperal fever recognise no other cause. Still more frequently are the surgeon or his assistants to blame, who have not very carefully cleaned their hands, or have used dressing material, especially instruments, not well disinfected.

In other cases contagion is explained by the persistence of morbid germs in rooms, on papers, tapestry, rugs, floor, and especially in clothing; sometimes also in vehicles which have served to transport patients. Hence the excellent measures taken for the disinfection of carriages and wagons. Disease may be transported also through letters. Graves's observation is well known: A young lady contracted scarlet fever through a letter which had been addressed to her by a friend of hers convalescent from this disease; the microbe had been transmitted through particles of scales falling from her hands. So in the isolation hospital of Aubervilliers letters are disinfected before they are sent to the post office: after perforating them by means of pins they submit them to the action of sulphur fumes.

Although less frequent, transportation through the atmosphere is undeniable. Intermittent fever is thus transmitted; the majority of cases of pulmonary tuberculosis acknowledge the same origin.

Lastly, the soil, and, above all, water are often contaminated with microbes proceeding from patients, and play a considerable part in the development of certain infections. It is through water that typhoid fever, cholera, and dysentery are propagated; it is in the soil that the germs of tetanus, gaseous gangrene, and anthrax spread themselves.

In cases of *auto-infection* there is no contagion; as already stated, the malady is generated spontaneously. Though the fact is of rare occurrence, it may be true as regards specific diseases, typhoid fever, for example. Military physicians have reported observations which seem to be absolutely demonstrative; soldiers have been seen to depart for manœuvres and lodge in villages where typhoid fever had not been observed for years past; in consequence of fatigue, a soldier is attacked by the fever, then another, then a third, and a small epidemic takes place. The same fact is observed in permanent camps; at the end of five or six weeks typhoid fever makes its appearance. A striking example is reported by Dr. Kelsch. During the war

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of 1870 the German army was camping on both banks of the Moselle; the contingent on the right bank suffered from typhoid fever in the proportion of only 12 per 1,000; the one on the left bank in the proportion of 27 per 1,000. Yet the conditions of air, earth, and water were the same, except that on the left bank there was more crowding, a greater mass of men, and therefore worse sanitary conditions. What seems to be still more conclusive is the fact that typhoid fever has been seen to make its appearance on board a ship five or six weeks after it had left the land. Certain authors, convinced contagionists, have doubted the reality of these facts; others have attempted to explain them by a very seductive theory. Drs. Rodet and Roux have argued that the typhoid bacillus is but a variety of colon bacillus, this common guest of our alimentary canal. If the resistance of the organism be diminished, the disease sets in, spontaneously in appearance, but in reality by the exaltation of this parasite until then inoffensive. This ingenious conception has occasioned a great number of contradictory studies. But to-day we no longer need such a hypothesis, as, according to Reumlinger and Schneider, the typhic bacillus is found in the intestinal contents and fæcal matters of persons in good health; this fact explains the apparently spontaneous development of the disease, and its future transmission by contagion.

Other well-defined infections may also appear spontaneously—for instance, diphtheria. Its development is perhaps explained by the presence, in the buccal cavity, of a bacillus designated pseudo-diphtheric, which is often considered to be an attenuated variety of the Loeffler bacillus. The question has been put even with regard to gonorrhœa. Straus published a case alleged to have occurred without any contagion. But it is not safe in such cases to trust the assertions of patients who, too often, are unwilling to confess how they have been contaminated.

It must be acknowledged that, even for diseases whose contagion is most frequently admitted, it is not always possible to discover the method of contamination. If a great number of persons attacked by measles, and especially by scarlet fever, were questioned, the majority would be unable to say where and how they contracted the germ of their disease. Hence some physicians think that scarlet fever, which they see occurring without any contamination, may originate spontaneously; they have attempted to eliminate this eruptive fever from the class of specific infections and to admit that it is owing to a common microbe—to streptococcus, for instance—which, according to their view, becomes exalted and acquires certain special properties; it preserves its new qualities for a certain length of time, and this explains the further propagation of the disease.

Nearly all of the infections that originate spontaneously—viz., without any contagion whatever—are due to common bacteria, which become more virulent when our resistance grows fainter. Thus staphylococcus, an habitual guest of the skin, gives rise spontaneously, as it were, to abscesses, boils, and anthrax; streptococcus, vegetating in the mouth, provokes erysipelas and sore throat; pneumococcus produces bronchitis, broncho-pneumonia, and lobar pneumonia; colon bacillus causes enteritis, or, making its way into the liver, induces suppurative angiocholitis, etc. Microbes thus become educated; they learn how to overcome the resistance of the organism, and in the end constitute particular races, apt to reproduce in others an affection analogous to or identical with the one which they have in the first instance provoked. Streptococcus, for example, which has acquired the property of causing erysipelas, will produce erysipelas by contagion. That which has determined angina, will reproduce angina. Although there are instances of a different evolution, it seems that, while being exalted, microbes acquire a certain specific power—that is, a certain aptitude for reproducing accidents of similar location and evolution. In this manner at the present day is morbid spontaneity explained, and the ulterior transmission of a first case, arising without any contagion, accounted for.

Causes Favourable to Infection.—We are thus led to investigate the causes which, by diminishing our resistance, permit the development of infections.

There is, first, a series of *extrinsic causes* in connection with *regions* and *seasons*.

In some countries a certain infectious malady prevails endemically; in others the disease can not become acclimated. Yellow fever, which fearfully ravages some countries of America, has never reached the Old World. If, perchance, a patient is found on board a ship arriving at a European port, no cases occur in the city.

In some instances the exotic disease gets a foothold, as is the case with cholera; at times it assumes a character of exceptional malignancy; such proved to be the case of measles transported to the Faroe and Fiji Islands.

The influence of the seasons has long been recognised. It has been indicated by Hippocrates, and is clearly brought out by modern statistics. In a general way, infectious diseases, notably eruptive fevers, are specially frequent from March to July; the minimum extends from September to December. During the hot season gastrointestinal manifestations are more frequently observed; during the cold season, thoracic disorders.

The hygienic condition of a country is a factor of obvious importance. The number of infectious diseases has considerably decreased

since the progress accomplished in the disinfection of lodgings and clothing, the creation of special hospitals for the isolation of patients, and the improvement of drinking water. Even typhoid fever has become less frequent.

Morbid aptitude varies considerably with different *races*. The negroes are immune from certain infections, as yellow fever; even the mulattoes are safe, and in countries where the disease is endemic it is customary to say that a drop of black blood is the best of preservatives. The negroes are likewise little subject to malaria. They are, on the other hand, very susceptible to tetanus, and much inclined to develop chancroids on the slightest suppuration.

The yellow race is predisposed to smallpox, which rages as an endemic; their susceptibility is so marked that it is not rare to see relapses of this infection.

Acute articular rheumatism is, so to say, allotted to the Caucasian race.

Predispositions and immunities no less remarkable may be noted among different peoples of the same race. The Anglo-Saxons are very liable to sudor Anglicus, and especially to scarlet fever. But what is more curious is that the sensibility of the English to scarlet fever is of recent date. Sydenham, who was the first to describe this infection, considered it as very benign, hardly deserving the name disease—" *vix morbi nomen.*" Graves also held the same view, but he, at a later period, saw the disease change its aspect and become very fatal. It is not right, therefore, to repeat that the gravity of scarlet fever is dependent on the race, since the disease was formerly benign. Nor can it be attributed to climatic modifications, for the English, when in France, are attacked by serious scarlet fever, while the French going to England develop a benign form.

Veterinary medicine, even more than human medicine, furnishes numerous instances of predisposition and immunity characteristic of race. Algerian sheep are refractory to anthrax, and the black sheep of Bretagne are immune from murr. This last example brings us back to human medicine. Dr. Landouzy has much insisted on the frequency of tuberculosis among those inhabitants of Paris who present the character of the Venetian type—that is, fine skin and reddish hair.

If we pass from race to *family*, we meet with similar facts. There are families in which tuberculosis, or diphtheria, or erysipelas is notably frequent, and we speak, of course, only of cases of infections which develop without family contagion.

There exist also numerous *individual variations*; persons have often exposed themselves to contagion, even to inoculation, without being contaminated. Vaccine has failed in a great number of cases.

So in laboratories we see from time to time an animal that resists, while others apparently similar, placed under identical conditions and inoculated in the same way, all succumb.

In certain cases individual immunity may be explained by what has been very justly called *insensible vaccination*. The inhabitants of Paris, for instance, do not, as a rule, contract typhoid fever; but individuals arriving from the country are often attacked by it. It is because Parisians, from infancy, have been little by little impregnated with the morbid germ; thus becoming progressively habituated, they have either experienced no disturbance at all, or symptoms too slight and vaguely characterized to be attributed to their true cause.

It is in this way we must explain the disappearance of epidemics; if the cases, at a given moment, grow less and less grave and more and more infrequent, it is because, little by little, the population has undergone an insensible vaccination. The incontestable immunity of physicians is due to no other cause.

We may ascribe to an analogous process the fact that an infection gradually loses its gravity in the course of centuries, or acquires an unusual malignancy when invading a population until then spared. Nothing is more interesting and instructive in this connection than the epidemics of measles of the Faroe Islands. The disease was imported there in 1846. Of the 7,782 inhabitants, 6,000 were attacked, only the old being spared. In 1875 the same disease invaded the Fiji Islands, and caused the death of 40,000 persons out of a population of 150,000.

The resistance and predisposition of certain subjects are sometimes explained by their heredity. The sons of an arthritic person are predisposed to a series of nutritive affections, but they are refractory, or at least less susceptible, to tuberculosis.

In certain cases, an individual comes into the world with an *innate* tendency, quite different from heredity; its cause is generally a particular state of the parents at the moment of conception, and the state of the mother during gestation. We have observed, for example, a man and a woman of uncommon strength who had had three children: the firstborn and the youngest were very well constituted and had inherited the temperament of their generators; the second was poorly developed, remained feeble, and at the age of twelve years contracted a tuberculosis of which he died. Why did this child present such an inborn diathesis? Why had not the hereditary characters been transmitted? Simply because at the moment of conception the father was convalescent from pneumonia, and this accidental sickness had sufficiently disturbed his organism to modify his progeny. Is there not in this observation, as conclusive as an experiment, the explanation of many a fact concerning family and race modifications?

The aptitude for contracting infectious diseases varies considerably with *age*. During intra-uterine life the fœtus is exposed to some diseases whose germs are transmitted through the placenta; such are especially syphilis, variola, septicæmia, exceptionally tuberculosis and typhoid fever. We shall again refer to these facts in the chapter on heredity.

At the time of birth the individual presents a sufficient resistance to the majority of infections: vaccine does not take, eruptive fevers are altogether exceptional, also typhoid fever and diphtheria. This immunity should not, however, be exaggerated; the newborn catches erysipelas very easily, which localizes itself usually in the navel and is almost invariably fatal.

It is especially during second infancy that infections are frequent. It may even be stated that at this epoch of life the tissues are particularly liable to let the parasites multiply. Pityriasis, for instance, has no hold on the aged and is spontaneously cured with the progress of years.

With age, the frequency of infectious diseases diminishes; in the old, hardly any but vesical infections and pneumonia occur. One might suppose that the immunity of old age depends upon previous maladies and insensible vaccinations. The explanation is unsatisfactory; a certain part must be played by the modifications developed in the chemical constitution of the tissues and humours. This view is supported by the fact that, when measles prevailed in the Faroe Islands, only the old were spared by the disease; in this case, insensible habituation is out of the question, since the disease was unknown up to that time.

The influence of *sex* is by no means less interesting. It seems that women are for a longer time than men predisposed to the infections of childhood. The eruptive fevers, notably varicella, extremely rare among men after twenty, are frequently observed among women between twenty-five and thirty years of age.

It is, above all, the different acts of genital life that give feminine pathology its peculiar character. Menstruation may be an occasional cause of infectious manifestations. Not to speak of herpes, whose nature is not well known, erysipelas, in some cases, appears at each period. Facts of this kind are seldom observed in hospitals, for menstrual erysipelas is benign; it lasts two or three days and hardly necessitates a cessation of work; it thus returns for years. Certain women may have as many as 50 and 60 relapses.

Pregnancy may modify the course of certain infections; in some cases it impresses them with a character of malignancy (infectious jaundice runs its course under the form of grave icterus); in other

cases it retards and may even momentarily stop their course. Not infrequently tuberculosis seems to stop, and, after confinement, the scene changes, the disease assuming a more rapid course. Last of all, we hardly need recall the frequency of puerperal infections. In this instance, however, the disease presents nothing special; the confined woman is in the same situation as a wounded one; it even seems, according to the researches of Straus and Sanchez-Toledo, that the uterus of the parturient opposes still a sufficiently strong resistance to infectious germs.

All violations of the laws of *hygiene* predispose to infections. We have already spoken of the noxious effects of great agglomerations. In intrenched camps infections are frequent; they are equally so in armies in the country. It is always the same diseases that occur: scurvy, dysentery, typhus fever. The frequency varies with wars—in the Crimea, out of an effective of 309,000 men, 75,000 suffered.

Crowding in prisons acts in the same way. Not many years ago deadly epidemics were of frequent occurrence in hospitals, decimating the convalescents; in the wards devoted to cases of measles, pulmonary infections propagated to the despair of physicians. Mortality has greatly diminished since isolation has been practised.

The influence exerted by *previous* or *actual diseases* is familiar. Some of them predispose to infections: Diabetes favours the development of pyogenesis of the tubercle bacillus; pneumonia, erysipelas, rheumatism, far from conferring immunity, predispose to new attacks. In most cases infections create a refractory state and prevent future attacks. But immunity is never absolute, save, perhaps, in the case of syphilis.

Among causes which intervene to lessen for a moment individual resistance, it is well to note fasting and fatigue.

The influence of *fasting* is evident; it is a matter of common observation, which has found a scientific confirmation in the experiments of Canalis and Morpurgo.

More interesting is the rôle of *overwork*. It has long been recognised by veterinarians that anthrax and glanders attack specially the overworked animals. It was once believed that excess of muscular work sufficed to create disease; it is known to-day that it only predisposes to infection, either by diminishing resistance to surrounding germs or by allowing the development of microbes contained in some point of the economy. That is what occurs in glanders; before the fatigue, the animal supported, without any disturbance, some rare nodes.

In human medicine examples abound. The fatigues imposed on troops lead to the development of various infections, from typhoid fever to tuberculosis. Do we not know that students of medicine do

not contract the infections to which they are daily exposed, except when they are weakened by fatigue or excesses? The overworking of an organ may even explain certain clinical forms. Cerebral rheumatism is rare in hospitals, because it occurs only in individuals addicted to intellectual activity, in those whose nervous system has suffered from late hours, excesses, ambition, and disappointments. Likewise, in young subjects, growing bones are predisposed to microbic localizations, as expressed by the development of osteomyelitis. Conversely, a nonactive organ does not present a rallying point for microbes; children suffering from mumps do not develop orchitis; this localization is not observed until after puberty.

External agents whose rôle we have already pointed out may intervene to favour the development of infections.

We have already stated that great traumatisms, lacerations, and extensive contusions considerably diminish resistance to microbes.

Inhalation of solid particles, such notably as silica and ferruginous dust, may produce small pulmonary erosions favourable to the development of tuberculosis.

Among physical causes are to be cited, first, *cold* and *heat*. The action of these two factors is really very complex, and it is not by modifying our bodily temperature that they act. The fact that the chicken, by nature immune from anthrax, contracts this infection when it is exposed to cold, and that, on the contrary, the frog loses its immunity when it is heated, is not due to the modifications of the organic temperature thus produced in these animals. The immunity of the chicken is not due, as some had believed at first, to the fact that the bird possesses a temperature too high to permit the development of bacilli, for the pigeon is not endowed with the same power of resistance. The frog is refractory to anthrax, not because its temperature is too low, for the toad contracts the disease. In reality the phenomena are more complex; when the chicken is exposed to cold or the frog to heat, a whole series of modifications are provoked: nutrition is disturbed, the life of the cells, and consequently the constitution of the humours, is altered, the nervous system, the heart, the leucocytes are acted upon. The abolition of immunity is the resultant of manifold factors.

It is also through a very complex mechanism that cold or heat occasions in man the development of infections. Cold, for instance, does not act by subtracting heat, for its influence is at times too quick. It is often said that by provoking a cutaneous anæmia it determines a visceral congestion, which weakens resistance. This theory is not plausible. It is well established to-day that active congestions, far from favouring, hinder infections; it is anæmia that diminishes the

means of protection. It is then probable that peripheric cold produces pulmonary anæmia, and that the blood is simply driven into the abdominal vessels; the congestion discovered after an attack of cold is already a reactionary phenomenon.

A good many of the *chemical substances*, including those known as antiseptics, diminish the resistance of the tissues and favour the development of microbes. So the tendency is in surgery to substitute more and more asepsis for antisepsis. General intoxications play the most important part. Numerous clinical and experimental facts demonstrate that alcohol, chloroform, and chloral promote the development of infections. The inhalation of deleterious gases has a similar effect; it favours general infection or the invasion of the lung. It is well known that broncho-pneumonia may be produced by carbonic oxide, as pulmonary gangrene by the gas of cesspools.

In being eliminated through the mucous membranes certain poisons destroy the epithelium and open the door to infectious agents. Mercurial stomatitis is due to the development of microbes contained in the mouth; hence the conception that it may be cured by means of antiseptics, by washing the mouth with the liquor of Van Swieten; hence also the possiblity of its being sometimes transmitted by contagion. The microbes of the buccal cavity are exalted to the point of overcoming the resistance of the normal tissues. The same mechanism presides over the development of mercurial enteritis; this is also a case where mercury, in being thrown off through the intestines, has simply facilitated the invasion of the mucous membrane by ordinary bacteria.

The more we study pathology, the greater we find the intervention of microbes in the majority of toxic processes. Hepatic cirrhosis is justly attributed to the action of alcohol; but it is possible that the poisons act simply by permitting the invasion of the liver by the microbes of the intestine; the sclerous process would be, in the last analysis, of infectious origin.

We must recall also that, of the causes already considered as favouring infections, not a few act by inducing auto-intoxications; diabetes, as well as overwork, are of the number.

One of the chief causes influencing infection is infection itself: there are microbes that invite each other, unite and help one another. We thus come to the study of microbic associations.

MICROBIC ASSOCIATIONS

Here is, in the first place, an experimental fact which is of a character to bring home to you the interest of the process.

Take a culture of *Bacillus prodigiosus*—namely, a simple saprophyte—remarkable only for the beautiful red colour it gives the me-

dium in which it develops. Inject a few drops of it beneath the skin of a rabbit; no trouble whatever will result. Then take a culture of symptomatic anthrax—that is, an anaërobic bacillus which produces in certain animals a gaseous gangrene (page 112); but the rabbit enjoys a natural immunity against this microbe, of which it can receive injections with impunity. Here, then, are two bacteria, both harmless for the rabbit.

Take now a third rabbit; inject into it a mixture of the two cultures: gaseous gangrene will develop and entail a speedy death. Thus, two microbes which, taken separately, are harmless, occasion a deadly disease when they are united. In this instance the microbe that favours the infection, *Bacillus prodigiosus*, acts by a soluble substance, which glycerine dissolves and alcohol precipitates, which resists a temperature of 120°, and, by all these characters, resembles peptotoxine. One drop of this injected into the veins of a rabbit of 2,000 grammes is sufficient to abolish its natural immunity.

Many analogous examples might be mentioned. Attenuated cultures of streptococcus or pneumococcus recover their virulence when they are mixed with the soluble products of *Bacillus prodigiosus* or of putrefaction bacteria; in the same way colon bacillus promotes the development of the typhoid bacillus.

So far the results are perfectly concordant; we shall see presently some complicated facts.

Let us take a culture of *Bacillus anthracis*—namely, of true anthrax, which should not be confounded with the symptomatic anthrax above referred to. We are now dealing with a microbe which is equally pathogenic both for rabbit and guinea pig. Let us inject into animals of these two species a few drops of an anthrax culture mixed with a living or sterilized culture of *Bacillus prodigiosus*. In the guinea pig the fatal termination will take place more speedily than if the anthrax culture alone had been injected; thus far the outcome is not surprising. In the rabbit, the anthrax infection will be thwarted and the animal will survive. Thus, the very same microbe, *Bacillus prodigiosus*, according to the agent with which it is associated and the animal which is operated upon, behaves altogether differently. This last result leads to a new conclusion: there are some microbes which hinder infection.

These experiments will presently enable us to interpret clinical facts.

Three different microbic associations may be observed in man: (1) Two infectious diseases develop side by side without influencing each other; (2) in some infections microbic association is the rule and

gives to the clinical tableau its peculiar aspect; (3) the superadded infection constitutes a true complication.

The first eventuality is realized when two eruptive fevers coexist in one individual. Measles, scarlet fever, varicella, and smallpox may combine without influencing one another; likewise, vaccine and small-pox may develop together, as may measles and whooping cough. Each disease runs its course on its own account, as if it were alone.

In other cases one disease starts, the other later follows it. To take a simple example, we shall cite vaccinal syphilis. Syphilis and vaccine are inoculated simultaneously; the vaccine pustule appears first, and when its evolution is over, instead of disappearing, it hardens and is transformed into a chancre. Likewise, the mixed chancre is due to the simultaneous inoculation of the viruses of chancroid and syphilis; the soft chancre, whose incubation is shorter, develops with its habitual features, and, later, is transformed into a hybrid lesion.

Cases of pneumo-typhus may also be mentioned. The mixed infection begins as a pneumonia; afterward, toward the ninth day, defervescence takes place, but, instead of being perfect, it is incomplete; the fever changes its type, the typhoid infection, masked until then by the pulmonary infection, becomes apparent, and from that moment runs its accustomed course.

Let us now come to the more interesting cases in which two microbes unite and constitute what is called, in natural history, a *symbiosis*. Thus, the germs of tetanus and of gaseous gangrene can not, if they are isolated, overcome the resistance of healthy tissues; they need the assistance of pus cocci, even simple saprophytes. That is just what happens when one is wounded by a dirty instrument; if the tetanus bacillus and that of gaseous gangrene are present, they will be able to develop only by the aid of the various bacteria that accompany them.

Another example is afforded by the study of smallpox. The specific agent of this disease is unknown, but it is evident that at a given moment the eruptive elements are invaded by pus cocci, markedly by staphylococci. The symbiosis is so very intimate that, if the organism be modified by a vaccination, the suppuration is cut short; the eruptive elements become crusty and heal, whereas in the nonvaccinated an abundant suppuration sets in. The mere fact, therefore, that resistance against one of the microbes is strengthened has sufficed to hinder the development of the other.

There are diseases in which microbic associations are well-nigh constant; they are almost inevitable when the process occupies parts largely exposed to the contact of air. In all the infections of the mouth the principal microbe is found united to numerous bacteria.

Diphtheria, for example, is never pure; in some cases the association of microbes plays but a very limited part and has hardly any effect on the final result, but none the less it exists. The same is true of the infections of the digestive canal: in cholera, typhoid fever, or dysentery the process is equally complex. Finally, in tuberculosis, at least at a certain period, numerous microbes invade the lungs and modify the clinical evolution: the tuberculous becomes a pyæmic patient.

The third eventuality is realized in the very numerous cases where a second infection ingrafts itself upon a principal disease; boils, suppurations, parotiditis, gangrenes—observed so often in the course of, and especially during convalescence from, grave infections—are due to common bacteria which have invaded the organism owing to the weakening produced by the chief disease. It is even possible that certain relapses are in reality only secondary septicæmias and not repetitions of the first infections.

We may cite also the secondary infections of gonorrhœa, notably the arthropathies, which are caused by the common pus cocci; the pneumonias of erysipelas, which are almost always owing, not to the principal agent, but to pneumococcus; the broncho-pneumonias of measles, the nephritis of scarlet fever, the endocarditis, arteritis, and phlebitis, which are, in the majority of cases, due to some superadded process.

The secondary infection may sometimes modify the evolution of the principal disease to such an extent as to create a clinical form altogether special. Such is the case with hemorrhagic smallpox, whose very peculiar symptoms are due to an additional septicæmia—namely, the intervention of streptococcus. No wonder if vaccination, under such conditions, is of little efficacy; it does not insure against the secondary infection.

These few examples, which could easily be multiplied, establish the fact that additional infections sometimes impart to the principal disease a particular course and a special character of malignancy; sometimes they represent simple complications, and sometimes explain the development of new manifestations wrongly considered as relapses.

Experimental pathology teaches us that, in some cases, microbic associations are able to exert a favourable action. Facts of this kind are very rare in human medicine; it is admitted, nevertheless, that in the malignant pustule the pus cocci that are found in the lesion hinder the development of the anthrax bacillus.

Erysipelas undoubtedly has sometimes exerted a favourable action; cases are known where, under its influence, lupus, ulcerating and chancrous wounds and tumours, particularly sarcoma, have retroceded and

healed. These facts have led to the application of inoculation with streptococcus, or injection of its toxines, to the treatment of these diseases. Some encouraging results have been reported. It seems that in all these cases the microbe of erysipelas acts by giving rise to an inflammation—that is, by stimulating the slow organic reaction.

Modes of Entrance of Microbes

Microbes can penetrate by a great number of ways: First, through the *skin*; and we may well begin by inquiring whether the unbroken integument does at all permit the passage of bacteria. As a rule, it does not, but there are some exceptions. Anatomists are often attacked by small pustules, which develop where there is not the slightest abrasion; the liquids of anatomical lacerations swarm with bacteria, which have been able to invade a hair follicle. Garré and Zuckermann, operating upon themselves, have spread over their skin cultures of *Staphylococcus aureus*; one of them developed an anthrax, the other a boil. Babes has likewise shown that the bacillus of glanders, incorporated with an ointment, passes through the skin of a guinea pig, at least when care is taken to rub the skin in such a manner as to facilitate penetration into the glands.

Whether there be any small wound or not, microbes invading the skin often give rise to local and innocent manifestations only. Such is the case with the anatomical tubercle, which is readily healed by a simple curetting followed by iodoformic applications. Other forms of cutaneous tuberculosis, including lupus, may give rise to terrible lesions, but, as a rule, scarcely disturb the health. The reason is, the bacillus does not find on the skin favourable conditions for development; the temperature is not high enough and the tissue is too dense.

The anthrax bacillus, even in the most susceptible animals, such as the guinea pig, often produces nothing more than a curable lesion. If a culture is spread on the excised skin, nothing but a little œdema results, and that finally passes away.

If the inoculation is made beneath the skin, the phenomena are quite different. Yet it is a fact that adipose tissue does not much favour the microbe; so that fat persons resist better than thin ones hypodermic injections of viruses. The profounder the inoculation, the greater are the chances for the infection to develop. The example of hydrophobia is, in this respect, altogether demonstrative.

The *mucous membranes*, even when healthy, are more easily penetrated by microbes than the skin. The tubercle bacilli can pass through the conjunctiva, the bronchial or intestinal mucous membrane, without leaving any trace of their passage; they proceed to locate themselves in the corresponding ganglia, in the neighbouring

serous membranes, and excite specific manifestations which can not be traced to their origin. In other instances reactionary lesions break forth; pneumonia is the expression of the effort the organism makes for preventing the passage of the pneumococcus.

Ingestion appears to be a less certain method of infection than inhalation. It is nevertheless through the alimentary canal that infection takes place in typhoid fever, in dysentery, or cholera, and sometimes, especially with children, in tuberculosis. Hence arises the question whether the meat of infected animals is fit for consumption. To-day this question may confidently be answered: When there is generalized infection, as in cases of anthrax and glanders, the seizure of the meat should be ordered. As regards tuberculosis, which is observed in 3.8 per cent of cattle slaughtered at Villette, the use of the meat is allowed when the lesions are local.

It has been asserted also that milk propagates tubercular infection; but this liquid contains no bacilli unless the mammary glands are affected or the infection is extensive; therefore milk seems to be less dangerous than had at first been thought; and is the less so as it is mixed with noncontaminated milk, for the dilution of the virus diminishes the chances of contagion.

Infection by the genito-urinary passages, if we except venereal diseases, such as gonorrhœa, syphilis, and soft chancre, is quite rare. Under normal conditions, microbes do not go beyond the navicular fossa in men. In women they are very abundant in the vulva and vagina. But when pathogenic agents, such as streptococcus, are introduced into this canal, the germicidal liquids secreted by the mucous membrane destroy all the germs within forty-eight hours (Menge). At the time of confinement the resistance of the genital organs grows still stronger. Straus and Sanchez-Toledo established that the anthrax bacillus, introduced into the vaginal canal of a female guinea pig having just brought forth little ones, produces no trouble whatever in this animal, by nature so sensitive to anthrax. In the human species resistance is as well marked, for puerperal fever is, on the whole, quite rare; it is altogether exceptional in the country, notwithstanding the fact that the parturients take very few antiseptic precautions.

The *serous membranes* represent another entrance, open at times to infection; but despite oft-repeated assertions to the contrary, they are very well defended. Hence the possibility of great surgical operations; for, in spite of all the precautions taken, morbid germs are always introduced; they are constantly found beneath the dressings. They are, however, in too small numbers to overcome the resistance of the organism.

Lastly, another passage for infection is the nervous system; the agent of hydrophobia propagates through the nerves, as has been admitted by Duboué, of Pau, on the basis of clinical experience, and as numerous experimental researches have demonstrated.

In this manner the virus reaches the nerve centres; therefore, the nearer the affected nerve is to the bulb, the shorter the period of incubation; and furthermore, the first manifestations will vary with the region primarily contaminated.

Protection of the Organism against Microbes

When microbes have passed the first barrier, and been introduced at some point of the economy, they will multiply and secrete injurious substances.

Then three results are possible.

1. The microbe is not virulent, the leucocytes rush up and soon destroy it. Sometimes spores persist for a certain time, as when *Bacillus subtilis* is injected, but they produce no disturbance.

2. If the microbe has a pathogenic action, a struggle is entered into at the point where the invasion is made; liquids are exuded, leucocytes come out of the blood vessels; a local lesion is formed which will endeavour to circumscribe the infection.

3. Lastly, when the microbe is very virulent, the organism is, as it were, struck with impotence; the cells which attempt to approach the pathogenic agent are repelled by secretions credited with a power called negative chemiotaxis; the local lesion is wanting; general infection is produced.

Whether or not a local lesion be created, the microbes penetrate always beyond their point of entrance, following either the lymphatic or the venous path.

If they get into the lymphatic vessels, they meet with ganglia which can stay their course. The function of these little organs is revealed by some experimental researches and numerous clinical observations.

In the course of the most diverse infections—acute, subacute, or chronic inflammations, suppurations, as well as anthrax, tuberculosis, or syphilis—we observe the swelling of the ganglia corresponding to the affected regions. Modifications take place in them, analogous to those occurring at the point of inoculation; the cells rapidly multiply, and, in acute cases, a very extensive periganglionic exudation is sometimes produced.

The lymphatic glands, especially in regions where they form chains, represent veritable fortresses which stop, finally or temporarily, the pathogenic agents.

The other lymphoid productions play a similar part. The fact is demonstrated with respect to the tonsils; it is equally certain for the closed follicles, isolated or agminate, that are found at the surface of our mucous membranes.

This conception can even be extended to the serous membranes. Anatomists have described in these membranes formations which, by their arrangement and structure, represent ganglia flattened out, as it were. Such an organ is, for instance, the great omentum. Direct experiment demonstrates the protective rôle of this membrane. To be convinced of this, extirpate the omentum in rabbits and guinea pigs. Later, after a period of a month or two, inject into the abdominal cavity of the animals thus operated upon a few drops of a virulent culture of *Staphylococcus aureus*; death supervenes in twenty-four hours, or at the latest within two or three days. Controls of the same weight, who, to make the conditions identical, have been subjected to a simple laparotomy, receive the same amount of culture and all survive.

It should not be concluded, however, that the suppression of the great omentum entirely destroys the resistance of the peritoneum. For the animals operated upon survive if they receive a very small dose of a virulent culture, or if an attenuated microbe be employed. In repeating the inoculation, however, we notice that the animal deprived of the omentum is growing thin and cachectic, and finally succumbs, while the control animals manifest no disturbance whatever.

The rôle of the omentum must be especially marked in the young, because, with years, a fatty infiltration occurs that diminishes its activity. It is, however, in children that the peritoneum is frequently threatened by microbes, which swarm in the gastrointestinal canal, and so often cause inflammations there.

Similar protective arrangements are likely to be met with in the other serous membranes; but no experiments have been undertaken on the subject.

Microbes invade the blood, either after having passed through the lymphatic glands or by directly penetrating into the capillaries or veins. If they enter by way of the stomach or intestines, they reach the portal vein and successively pass through the liver, right heart, lungs, and left heart, to be thrown thence into the general circulation. In all other cases they pass first through the lungs.

No matter by what way they enter, the microbes that have reached the general circulation rapidly disappear from the principal vessels; at the end of ten or fifteen minutes they are no longer found in them, even when intravenous inoculation has been practised on the animal. The blood then represents an inhospitable medium for bacteria, which must abandon it and take refuge in the capillaries of the organs.

Here the battle between the organism and the pathogenic agents is fought out; the latter begin to multiply and secrete toxic substances, which should insure them victory, while the cells of the body endeavour to exert their protective rôle, either by manufacturing germicidal or antitoxic products, or by picking up and digesting the microbes.

Two hypotheses are possible. It may be assumed that the various phases of the struggle are alike in all the capillaries; in which struggle, as the case may be, the microbe or the organism would triumph, and the ultimate result would be the sum of the partial results of the same character. Or it may be supposed that the phenomena vary from one capillary network to another; that the effects of the struggle are not the same in all the organs, but in some of them the microbe is victorious, in others the cell. If so, the phenomena become more complex; the final result will be the sum of the partial results of the different kinds.

These theoretical considerations lead to the question whether there do not occur differences in the evolution of infectious diseases according to the vessel by which the culture is introduced.

Protective Rôle of the Organs.—In most cases the experimenters inject the microbes through some peripheral vein; then the pathogenic agent first passes through the capillaries of the lung, to reach afterward the general circulation. In order to bring out clearly the rôle of the pulmonary capillaries, an injection must be made at the very origin of the aorta; for this, it suffices to introduce a cannula by the central end of the right common carotid. The differences which will be presented by the development of the disease in the two cases will enable us to appreciate the function of the lung.

In other experiments the injection will be made by a branch of the portal vein to ascertain the action of the liver; by the distal end of the carotid artery to study the influence of the brain; by the femoral artery to notice what occurs in the less highly organized tissues.

The results vary with the microbes employed.

With anthrax cultures the animals inoculated by the aorta succumb first; those injected through the peripheral veins survive a little longer, which indicates a slight action on the part of the lungs. But this protection is of little importance and vanishes when the virus is very active. Lastly, the injections made by the carotid allow a survival somewhat longer than the intravenous inoculations. Thus far the differences are not considerable: if some animals resist longer than others, all succumb ultimately.

Altogether different are the results when the anthrax passes through the liver; thus, out of twelve animals having received con-

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siderable doses of anthrax culture by the portal vein, only three have succumbed. The liver, then, has the property of arresting and killing the anthrax bacteria; it plays a very important part in the protection of the organism against anthrax infection. With a very virulent culture, a dose of half a cubic millimetre injected through a peripheral vein kills a rabbit of 2 kilogrammes in thirty-eight hours. A dose of 8 cubic millimetres introduced through a portal vessel is incapable of killing a somewhat smaller rabbit. That is to say, a quantity of anthrax bacilli 64 times that which is fatal by the peripheral veins is completely annihilated by the liver.

The *protective action of the liver*, which is so conclusively shown by these experiments made with the anthrax bacillus, is just as easy to demonstrate with the *Staphylococcus aureus*.

Let us take a virulent sample, and, after diluting it in bouillon, inject it, as we did anthrax, through five different vessels. Contrary to the preceding results, the animals inoculated through the distal end of the carotid artery succumb first; the brain therefore represents an excellent medium of culture for staphylococcus. Next, the animals injected through the aorta or femoral artery perish. Those that have received the virus through peripheral veins survive longer; those that have received it by the portal vein resist inoculation. However, the liver acts with less energy upon staphylococcus than upon the anthrax bacillus; it neutralizes 8 fatal doses, instead of 64.

If we now pass to streptococcus, we find quite different results. The liver has no longer any power of protection; the microbes find in its parenchyma excellent conditions for vegetation, and animals injected through the portal vein are generally the first to succumb. A little later die those that have been inoculated through the aorta, the carotid, or the femoral artery. As to animals injected through the peripheral veins, they die slowly, or, if the virus be not a very active one, they may survive.

The lung then represents a protective organ against streptococcus; it fulfils a rôle analogous to that exercised by the liver against *Bacillus anthracis* or *Staphylococcus aureus*, except that it destroys pathogenic agents with less energy; the lung hardly nentralizes more than one deadly dose.

With colon bacillus the results are very variable. Experimenting with a microbe drawn from dysenteric stools, we have found a manifest action of the liver. On the contrary, in previous researches, pursued with another sample, the animals inoculated by the portal vein or the carotid artery succumbed first. The liver, far from destroying this microbe, affords it an excellent medium of culture. This result, while very deceiving from a teleological point of view, accounts well

for the frequency and gravity of hepatic infections of gastrointestinal origin.

With the bacillus of dysenteriform enteritis, the results vary with the age of the culture. If the culture is recent—viz., if it is four or five hours old—it does not yet contain any toxines; the liver then exercises a protective rôle: it arrests and destroys the microbe. If the culture is several days old, toxines have been produced in abundance; they annihilate the action of the liver and alter this gland; consequently the animals inoculated through the portal vein succumb first. Thus the liver acts upon the bacillus; it destroys the figurate element, but has no action upon its products of secretion.

Similar differences are observed in studying parasites of a higher order. Thus with cultures of *Oidium albicans*, the animals injected through the carotid perish first. The lung retards very slightly the course of the infection. The liver and kidneys arrest great numbers of the parasites and prevent the extension of the process; they protect the economy very efficiently.

The various results above indicated are summed up in the accompanying tabular representation (page 154), showing in what order the animals succumb, according to the mode of introduction of the microbes.

In brief, microbes injected in a blood vessel stop, in great numbers, within the first capillary plexus they enter. This is perhaps but a mechanical phenomenon of molecular adhesion comparable to that which, in a porcelain filter, prevents the bacteria from passing through pores larger than themselves. It may be, however, that a vital process is called into play, an action of arrest exercised by the endothelium, for analogous phenomena occur when, instead of figurate elements, soluble substances are introduced; injections made through different parts of the vascular system prove equally well the action of the organs both on poisons and on microbes.

In both cases the most important rôle is that played by the liver. The action of this gland, however, is not exercised indiscriminately upon all the substances or all the bacteria that reach it; there are poisons which the liver retains and transforms, others which it allows to pass, and still others which seem to acquire in its interior an increase of activity. This is at least what results from the experiments of Teissier and Guinard on the diphtheria toxine.

For microbes the results are the same: some stay there and perish, such as *Bacillus anthracis*, the staphylococcus, the bacillus of choleriform enteritis, the oidium; others, as the streptococcus and colon bacillus, easily develop there and grow stronger.

The action of the liver is more marked on microbes than on poi-

		Anthrax Bacillus.	Staphylococcus.	Streptococcus.	Colon Bacillus. First sample.	Colon Bacillus. Second sample.	Oidium.
Death	Very rapid	Aorta.	Carotid.	Portal vein.	Portal vein.	Peripheral veins.	Carotid artery.
		Femoral artery.	"	"	Carotid artery.	"	"
	More or less rapid, but constant.	Peripheral veins.	Aorta.	Aorta.	"	"	Aorta.
		"	Femoral artery.	Carotid artery.	"	"	"
		Carotid artery.	"	Femoral artery.	"	"	"
	Inconstant	"	"	....	....	....	
		"		....		....	
		"		....			Peripheral veins.
Survival	Frequent	Portal vein.	Portal vein.				Portal vein.
	Almost constant.	"	"			Peripheral veins.	Renal vein.

sons. When a toxic alkaloid is injected through a portal branch, the animal experimented upon is killed, provided the dose introduced be double that which is fatal by way of peripheral veins. As to microbes, we have seen that the liver arrests 64 fatal doses of anthrax and 8 fatal doses of staphylococcus. Its action is then much more important, or at least more marked, in infections than intoxications.

Furthermore, experiments demonstrate that other organs may also serve to protect the organism against infections. Such is the lung, which acts in a certain measure on the bacteridia of symptomatic anthrax and upon the staphylococcus, and exerts an action still more efficacious upon the streptococcus. Moreover, the kidney can retain the oidium and prevent the dissemination of this parasite.

We see, furthermore, from the experiments above reported, that blood is not a hospitable medium for microbes; the few which succeed in passing through the first capillary network do not circulate long; they lodge in the various organs, so that in a few minutes the blood again becomes sterilized.

The localization of bacteria is controlled by the following three conditions: The mode of entrance, of which we have sufficiently shown the importance; the physiological and pathological conditions of the organs, of which we shall presently say a few words.

The Causes which Explain Microbic Localizations

Bacteria which have passed through the capillaries of the first organ encountered, and which circulate for a moment in the blood, have a great tendency to settle in parts endowed with a strong nutritive or functional activity. In the young they stop in the growing bones; but they always spare those organs, such as the testicles and ovaries, which have not yet entered upon active life. In the case of an individual who has overtired an organ—the brain, for example—the localization will take place in that organ.

It is possible to fix at will the microbes in this or that part of the organism by producing traumatic or other lesions; by weakening the resistance of a tissue we favour its colonization by pathogenic agents. We have already mentioned the well-known experiment of Max Schuller: a traumatism at the knee of a guinea pig is followed by the development of a white swelling (*tumeur blanche*) if, at the same time, tuberculosis be inoculated. Clinics abound in similar examples. Parents always trace the beginning of a coxalgia, a tubercular meningitis, or a Pott's disease to a blow received by their child or to a fall. The observation is often just; but the blow or the fall is not responsible for the lesion; it has only favoured the development and localization of tubercle bacilli, which were already present in the organism.

When microbes are localized in an organ or tissue, the struggle begins. The final result will depend upon the forces of each of the two parties present. It is readily understood that all causes disturbing the state of health—various mechanical, physical, chemical, or animate agents; bad nourishment, fasting, overwork, excesses—in a word, all the conditions which we have found to be favourable for the development of infections, are also those that will render their evolution more serious.

In the case of microbes, we must first consider their *number*. It is altogether exceptional that a single microbe should be able to produce a disease, though the case may be realized with extremely virulent anthrax cultures: one bacteridium kills a young guinea pig. In most cases, to overcome the resistance of the organism, large numbers of microbes are required. Thus the guinea pig, of all animals the most susceptible to tuberculosis, does not catch the infection unless 820 bacilli are introduced beneath its skin. This figure may already seem quite considerable; but with the pyogenics the required numbers are much greater.

Operating with *Proteus vulgaris*, Watson Cheyne states that 5,000,000 to 6,000,000 microbes injected beneath the skin do not produce any lesion; 8,000,000 cause the formation of an abscess; 56,000,000 give rise to a phlegmon, to which the animal succumbs within five or six weeks; to cause death within twenty-four or thirty hours, 225,000,000 must be injected.

The same author has studied the action of the staphylococcus upon the rabbit: for producing an abscess, 250,000,000 microbes are required; for causing death, one milliard (1,000,000,000) is the requisite number.

In all these experiments the microbes were injected beneath the skin. By varying the mode of entrance, different results are obtained. To occasion suppuration by *Staphylococcus aureus*, it has been necessary, in the researches of Herman, to inject 4 to 5.3 centimetres of the culture into the peritoneum, 0.75 to 1 beneath the skin, 0.25 into the pleura or arachnoid, 0.05 into the veins, 0.0001 into the anterior chamber of the eye. The anterior chamber is then the least protected part of the organism. The same is demonstrated also by the study of symptomatic anthrax; this virus, harmless for the rabbit when injected hypodermically, causes speedy death when introduced into this part of the eye.

The figures given by the authors have of course but a relative value; for *virulence* differs much with different samples and its variations constitute undoubtedly the most important factor that we have to study.

Microbes become attenuated when they are kept outside of the organism. In our artificial cultures they rapidly lose their virulence. We can even hasten their attenuation by placing them in unfavourable media. By maintaining the culture at too high a temperature, by subjecting it to the action of compressed oxygen, by adding to the medium antiseptic substances, we can reduce its pathogenic power progressively.

To increase the virulence, we must reverse the conditions—make inoculations in animals, cultivate the microbe in favourable media, above all in bouillon to which some blood serum or liquid of ascites is added. The procedure of inoculations in series, already employed by Davaine, has enabled this scientist to obtain a virus sufficiently active to kill guinea pigs into which one millionth of a drop was injected. Similar facts are observed in clinics. One of the parasites which we carry, pneumococcus, for example, when exalted, gives rise to pneumonia; it then can by contagion infect a second person, and, thus transmitted, produce a little epidemic. Let us note, however, that a microbe exalted for one animal species is not necessarily so for others; every day we see streptococci having caused mortal diseases in man prove hardly pathogenic at all for animals. We have studied a sample of anthrax which, after successive passages in rabbits, had become, contrary to the rule, far more virulent for this animal than for the guinea pig.

CHAPTER IX

GENERAL PATHOGENESIS OF THE INFECTIOUS DISEASES

The mode of action of microbes upon the animal organism—Importance of microbic toxines—Putrid poisons—Poisons produced by pathogenic bacteria—Principal bacterial toxines—Toxines produced by nonbacterial infectious agents—Mode of action of toxines: reactions excited by them.

In order to understand in what manner microbes accomplish injury to the organism, three principal hypotheses have been advanced.

The first, which no longer has any but an historical interest, assumed that an obstruction of the capillaries by bacteria occurred. It was a mechanical theory.

Secondly, a struggle for life was assumed. It was held by those entertaining this view that the microbes and cells vied with each other over the alimentary materials carried by the blood and lymph. Whichever of the two elements succeeded in appropriating the most, reduced the other to starvation.

The third and modern conception seems to be established in indisputable proofs, and regards the infectious process as an intoxication. According to this view, the microbes act through the agency of the soluble substances which they contain or elaborate.

PUTRID POISONS

Before the pathogenic microbes were known—i. e., at an epoch when the animate nature of putrefactive agents was not even suspected—important results had already been obtained.

In 1758, Seybert demonstrated that the putrefaction of pus, serum, and infusions of meat developed in these fluids a high degree of pathogenicity. At the beginning of the present century the remarkable researches of Gaspard, completed by Magendie, Virchow, Stich, and especially by Panum, conclusively established the existence of putrid poisons.

The substances originating in the course of putrefactions are very great in number. Gases, fatty acids, aromatic substances, and amido

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bodies are encountered, which, however, are not sufficiently numerous or active to be taken into account. Next, we meet with albuminoid substances and bases analogous to vegetable alkaloids. Panum admitted that putrid poison was of an albuminoid nature; on the other hand, most authorities held a contrary view, and their opinions seemed to be definitely established by the results obtained through the researches of Gautier, Selmi, and Brieger. The putrefactive bases were called *ptomaines* (Selmi), or, what was etymologically more correct (πτῶμα, πτῶματος, cadaver), *ptomatines* (Kobert).

A great number of cadaveric bases are now known.

Some of these substances are chemically well defined: methylamine, trimethylamine, triethylamine, propyl, butyl, amylamine, neuridine, saprine, cadaverine, putrescine, neurine, choline, gadinine, collidine, etc. Others are distinguished by their toxicity, and are sometimes named according to the analogy of their action with that of certain alkaloids—e. g., mydaleine, ptomatropine, ptomatomuscarine, ptomatocurarine, ptomatoconicine, ptomatoveratrine, tyrotoxine, etc.

Ptomaines differ notably according to the time at which the products of putrefaction are studied. Some appear and later disappear, to be replaced by others. The chemical researches which have made us acquainted with these results, however interesting they may be, should have been completed by bacteriological researches. It is a question whether these different ptomaines are produced at the various phases of life of the same microbes, or whether their successive appearance and disappearance depend upon different microbes, which destroy or transform the substances already produced by their predecessors.

Even though we do not exactly understand the rôle of ferments in the genesis of ptomaines, we are better acquainted with the part played by the media in which they are produced. We know that certain bases are encountered in all putrefactions—for example, neuridine. On the contrary, neurine is found only in the putrefaction of the flesh of mammalia, and muscarine only in the putrefaction of the flesh of fish. Similarly, it is at the expense of fish that gadinine, ethylendiamine, and trimethylamine are formed. Dimethylamine has so far been found only in the putrefaction of gelatine or of yeast. Tyrotoxine is the poison which is formed in decomposed milk and cheese.

Drs. Kostiurine and Krainsky very justly remark that the toxicity of the products of putrefaction is in direct ratio to the chemical complexity of the matters undergoing putrefaction—e. g., more poison is yielded by meat than by bouillon, and more by bouillon than by saline solutions, indeed, the latter not yielding any.

Thus far all the results seem to harmonize and to lead to the admission that the putrid poisons are of alkaloidal nature. There has

been some question, however, whether this conclusion was justified. Chemists have been reproached with having created, as it were, the substances they isolate, or at least with having dissociated the true toxic molecule, which is more complex and unstable. The ptomaine, it is objected, does not pre-exist in the putrid liquid; it enters into the constitution of a proteid substance, from which it is driven by analytical procedures. The true poison, therefore, is an albuminoid. In favour of this view may be mentioned a great number of researches demonstrating that when putrid matters are treated with alcohol the substances precipitated by this solvent are the most toxic. The question, therefore, is deserving of further investigation, which would probably lead to the discovery in putrid matters of toxines, some belonging to the group of toxalbumins and others to the peptotoxines and toxalbumoses.

Poisons produced by Pathogenic Bacteria

The putrid poisons are of great interest, not only because some are constantly formed in the digestive canal, as has already been stated, but also on account of the fact that their study is a suitable introduction to the history of the poisons produced by pathogenic micro-organisms.

Davaine thought that the anthrax bacillus secreted a substance which agglutinated the red blood corpuscles, and Pasteur confirmed this hypothesis in studying the effects of filtered anthrax blood. Toussaint, Chaveau, and especially Gautier, argued in favour of toxic secretions of bacteria. Pasteur finally offered a basis of demonstration by establishing the fact that filtered cultures of the bacillus of chicken cholera produced transitory somnolency in birds—i. e., it reproduced one of the symptoms of the disease. This symptom, however, was of no particular interest, and Pasteur therefore refrained from concluding that the microbe acted by toxines.

The idea of a microbic intoxication was, however, fully accepted when it was demonstrated that infectious agents are capable of provoking a fatal disease even though they remain localized at some point of the organism. Loeffler sustained this hypothesis with reference to diphtheria; Koch accepted it as regards cholera, and there was no logical escape from its adoption with regard to tetanus, symptomatic anthrax, and emphysematous gangrene.

Then Brieger, prepared as he was by his studies upon ptomaines and putrefaction, extended his researches to pathogenic microbes. In the impure cultures of tetanus bacillus with which he worked, and in those of typhoid bacillus, he found various ptomaines which he studied from the standpoint of chemistry and toxicology. From that moment

the way was open. Investigators hastened to engage in research and described a great number of toxic bases of microbic origin.

Serious objections, however, were soon raised. It was pointed out that the ptomaines as extracted from cultures are far less powerful than the total cultures, and fail to produce the same phenomena. Pursuing the study of microbic poisons, it was recognised that the most active substances, as in the case of putrid poisons, are not soluble in alcohol, but precipitated by it. The tendency was then to attribute the toxicity of cultures to substances considered successively as ferments, peptones, albumoses, toxalbumins, globulines, proteines, nucleo-albumins, etc.

The idea of comparing the microbic toxines with ferments is based on chemical and toxicological facts. Like ferments, (a) toxines are precipitated by alcohol; (b) adhere to precipitates of calcium phosphate which are produced in the liquids containing them; (c) are destroyed by heat; (d) they act in infinitesimal doses. This comparison is acceptable, especially at the present day when there is a tendency to consider the fermentative power as a physical property of matter; the albuminoid substance serves simply as the substratum of a mode of energy. That it may be deprived of its power by means of various procedures, notably by heating, is quite conceivable. The conditions would be the same as in the case of a magnet. The magnetic property is one of a physical order; the magnetized iron has no special chemical constitution. With this conception the ferment is a complex material which has received from the living substance a certain degree of energy, possessing, as it were, a part of vital activity. It is said by Buchner to be a semiliving substance. At any rate, it is the highest expression of matter destitute of life. Thus understood, the action of toxines is no more mysterious than that of ordinary ferments.

What render the study of microbic toxines more difficult are the varying results obtained according to a great variety of circumstances, in but few of which precision is possible.

The action varies with the same microbe according to different samples. As a rule, it increases as the virulence becomes greater.

The effects are modified in the same sample according to the culture medium. The more complex the medium, the greater the amount of toxines produced. In this respect nothing is as good as the natural organic fluids, such as blood serum and ascitic fluid, under which conditions virulence is best preserved.

In the same culture toxicity varies with age—i. e., with the time elapsing since the inoculation. Very often it increases steadily with age; in other instances the reverse is true. No definite rules can be

formulated in this respect any more than with reference to the action of heat or air. The diphtheria bacillus, for example, produces more poison in well-aerated bouillon, while the reverse is true of the streptococcus.

The variability of the results depends partly upon the plurality of toxines. In fact, there are toxic substances which exist in the bodies of bacteria. These are the *proteines* or *nucleo-albumins,* which are diffused in the medium when the culture grows old—namely, when the microbes are destroyed and disintegrated. On the other hand, the medium contains substances which are in part due to a secretion of the bacteria themselves. Others are formed either by destruction of nutritive materials or by synthesis. These are the *toxalbumins,* the *toxalbumoses,* and the *toxopeptones.* As to the ptomaines, they are gradually being recognised as derivatives of true toxines.

When introduced into a living organism, toxines do not at first produce any disorder. A period of latency elapses, varying from a few hours to several days, before the appearance of morbid phenomena. On the other hand, with the poisons derived from true toxines—for example, the ptomaines—the manifestations are of immediate occurrence, exactly as is the case when a vegetable alkaloid is injected. It has therefore been supposed that the primary poison is decomposed in the organism and parts with its toxic radical. This hypothesis is apparently quite plausible, since alkaloids are found in the urine; at any rate, substances which have an immediate action are detected there. However, this conception should not be admitted in all its simplicity, for the phenomena are probably more complicated, and the total toxine has perhaps already caused profound modifications in the organism.

In general, it is difficult to say what are the phenomena provoked by toxines. The manifestations evidently vary from case to case. However, the events may be divided into three groups:

(*a*) Some are seen at the point of introduction of the substance; these are the local manifestations.

(*b*) Others express the impregnation of the entire economy; these are the general manifestations.

(*c*) Finally, others point to a selective action on certain organs, apparatus, or tissues.

Toxines may provoke at the point of introduction a lesion similar to that produced by the agent from which they are derived. First an inflammatory œdema is produced. For example, the erysipelas poison, like the living streptococcus, produces œdema in man as well as in animals—a fact convincingly manifested in subjects into whom sterilized cultures of streptococcus were injected for therapeutic purposes.

Next, we have the suppuration so easily produced by the soluble products of the streptococcus, staphylococcus, and gonococcus. Dr. Christmas injected into a normal urethra a trace of gonococcus toxine and produced a purulent discharge, which, however, disappeared within a few hours, as he did not continue to deposit the irritating substance on the mucous membrane.

Likewise, the necrosis characterizing gangrene is induced by soluble products, as is proved by subcutaneous injections of toxines derived from the bacillus of emphysematous gangrene. The same is true of pseudo-diphtheritic membranes, which may be produced by introducing into the trachea a few drops of the toxine generated by the Loeffler bacillus.

In this manner all the local processes attributable to microbes can be reproduced by means of the toxines freed of the living germs. The general phenomena are due to the same mechanism. The injection of soluble products gives rise to fever with all its consequences— e. g., variations in combustion, respiration, and urinary secretion. When sterilized cultures of streptococcus are injected into man for therapeutic purposes, fever results, ushered in by chills and attended by general depression, dry tongue, and, in some cases, an often abundant outbreak of herpes labialis.

The introduction of strong doses or repeated injections of toxines give rise to cachexia similar to that induced by prolonged infectious processes. Diarrhœa sets in, the cells of the organs degenerate, and death ensues from marasmus. In this respect the toxines of the tubercle bacillus are very interesting; they act like the microbe from which they are derived.

If the course is slower, the manifestations may predominate in a viscus, thus constituting an affection which sometimes begins, and in most cases continues, long after the toxine injections have been suspended. In this way it is possible to reproduce visceral sclerosis, hepatic cirrhosis, nephritis, myocarditis, as well as paralysis and muscular atrophies often due to medullary lesions, predominating in the large cells of the anterior horns.

Thus, toxines can reproduce all the lesions induced by microbes. We may, therefore, conclude that infection is but a chapter of intoxications.

Since microbes give rise to toxic substances during the course of diseases which they originate, some authorities have entertained the idea of searching for these poisons in the organism of the sick. The labours of Rumo and Bordoni have established their presence in the blood; Professor Bouchard's experiments have demonstrated their passage into the urine. It should be remarked, however, that the phe-

nomena are in reality very complex.   In an infected organism three kinds of poison are encountered:

(*a*) The microbic toxines, engendered by the pathogenic agent.

(*b*) The putrid poisons, originating in the intestine, where fermentations are often more intense than normally.

(*c*) The cellular poisons, due to disturbance of assimilation, which is exaggerated and vitiated.

If, in addition, the organs destructive to toxines are altered and incapable of fulfilling their rôle, which is often the case, we can understand how the sources of intoxication are multiplied. If the organism resists, it is owing to the fact that part of the toxines constantly escapes through the emunctories, notably by the kidneys; the urine becomes hypertoxic, and this hypertoxicity is a safeguard for the economy. In many cases, however, there is a greater complexity of phenomena. In pneumonia, for instance, the urinary toxicity grows less as the disease progresses; the poisons accumulate in the organism, to be suddenly thrown out at the moment of defervescence; a urinary crisis is then observed, characterized by a strong polyuria and a toxicity of the urine, which may exceed from five to six times the normal toxicity.

The Principal Bacterial Toxines

Not wishing to describe the microbic toxines thus far studied, we believe that it would be interesting to sum up in a few lines our present knowledge of the principal toxines.

We must first consider those infections whose mechanism is inexplicable otherwise than by admitting the action of a soluble poison. We here refer to those infections whose agent remains at the point of inoculation—e. g., diphtheria, tetanus, cholera, emphysematous gangrene, and symptomatic anthrax.

Diphtheria.—The diphtheritic toxine, discovered by Roux and Yersin, can be obtained in such high degree of activity that $\frac{1}{50}$ and even $\frac{1}{500}$ of a cubic centimetre kills a guinea pig of 500 grammes weight. If we remember that 1 cubic centimetre of the fluid gives 1 centigramme (0.01) of dry residue, say 0.0004 of organic matter, and that the toxine represents but one part of this matter, we are led to the conclusion that it can poison a living being 20,000,000 times greater than its own weight!

The active principle, insoluble in alcohol, is destroyed by light, heat, oxidizing agents, iodine water, and trichloride of iodine. Roux and Yersin hold it to be a ferment; Brieger and Fraenkel, a toxalbumin; Wassermann and Proskauer, an albumose, or, at least, intimately united with an albumose.

All living beings are not equally susceptible to the diphtheritic poison. Animals which are refractory to the living bacillus are equally so to the toxine.

Of the animals easily poisoned we must mention the guinea pig. The rabbit is quite resistant, the dog much more so, and the mouse and the rat endure high doses.

Subcutaneous injection produces œdema in the guinea pig and causes death within two or three days. The post-mortem changes noted are pulmonary congestion, pleural effusions, and hemorrhages in the suprarenal capsules. In the rabbit the predominant feature is cellular degeneration of the liver and kidneys.

When deposited upon the surface of even a healthy mucous membrane the diphtheritic toxine gives rise to the formation of false membranes. In animals this result has been obtained in the larynx, the conjunctiva, and mucous membrane of the vulva.

Injections of very small doses may give rise to paralysis with changes in the nervous system and myocarditis.

Tetanus.—In the early studies of tetanus complex methods were employed. These were subsequently replaced by simpler procedures. Brieger isolated a whole series of bases : tetanine, tetanotoxine, spasmotoxine—all three convulsivants, and one base stimulating the salivary and lachrymal secretions.

These bodies act only in enormous doses. In fact, the true poison is an albuminoid substance discovered by Knud Faber, and studied by Brieger and Fraenkel, Tizzoni and Cattani, and especially by Vaillard and Vincent.

The poison obtained by filtration of the cultures is of such activity that $\frac{1}{100000}$ of a cubic centimetre suffices to kill a mouse. Injected beneath the skin, it causes tetanus after a variable period of incubation. According to Courmont and Doyen, the poison acts indirectly ; it causes the organism to produce a tetanizing poison. This very ingenious hypothesis has been the subject of lively discussions and can not as yet be considered as absolutely established. Two theories have been advanced to explain the mechanism of convulsive phenomena : Autokratov, Courmont, and Doyen admit an action of the poison upon the sensory nerves ; Brunner admits a modification of the spinal cord similar to that produced by strychnine.

Cholera.—The choleraic poison has been successively studied by Petri, who considered it a toxopeptone ; by Hueppe and Scholl ; by Gamaléia, who regards it as a nucleo-albumin contained in the bodies of the bacteria ; by Sanarelli, Brieger and Fraenkel, Pfeiffer, and especially by Ransom. Ransom's researches, completed by those of Metchnikoff, Roux, and Salimbeni, demonstrate that the cholera poison, un-

like the preceding ones, resists boiling. Injected into animals, it produces prostration, meteorism, and diarrhœa; death supervenes with hyperpyrexia. At the autopsy, hyperæmia of the intestines, peritoneal effusion, and congestion of the liver, kidneys, and, in the guinea pig, of the suprarenal capsules are found.

Gaseous or Emphysematous Gangrene.—The toxine of emphysematous gangrene, prepared by Besson, produces œdema, which is often followed by a slough.

In symptomatic anthrax there is found a toxine which was pointed out by Duenschmann.

We now come to the group of microbes which have a tendency to invade the entire organism. Their chief representative is the *Bacillus anthracis*.

Anthrax.—Considered as a ptomaine (Hoffa), a toxalbumin (Brieger and Fraenkel), an albumose (Sidney Martin), the anthrax toxine has been well studied by Marmier. It is primarily found in the bodies of the bacteria, and remains inclosed therein if the culture is made under favourable conditions; if not, it abandons them and is diffused in the surrounding medium. Injected into animals, it produces fever and diarrhœa, and causes death by hyperpyrexia and final convulsions.

This poison resists heat quite well; it is attenuated by hypochlorites and the iodo-iodide reagent.

Septicæmia.—It is to the group of bacilli producing hemorrhagic septicæmia that the microbe of chicken cholera belongs. We have already referred to Pasteur's experiment upon the narcotic poison contained in bouillon cultures. It may be well to mention some researches demonstrating that the various microbes of this group likewise produce toxic albuminoids (Schweinitz, Voges).

Similar demonstrations have been made regarding the *Bacillus proteus vulgaris*, *Bacillus pyocyaneus*, and *Bacillus septicus putidus*.

Colibacillosis.—The important part played by the colon bacillus group, even in normal states of the organism, renders necessary a special mention of it in the rapid review here presented.

The soluble products of the microbes belonging to this group have been studied by Denys and Brion, and especially by Gilbert. Their action is the more marked the stronger the virulence of the germ employed and the older the culture. Nevertheless, to bring about a fatal termination, quite high doses are generally necessary, varying from 37 to 74 cubic centimetres per kilogramme. In the animals under experiment the result is very marked nervous phenomena, notably tetaniform convulsions.

With a sample derived from dysenteric stools, we obtained an

extremely active toxine: a dose of half a cubic centimetre injected into the veins of a rabbit of 2 kilogrammes weight caused death with an intense diarrhœa and fever. Greater doses, as high as 15 to 20 cubic centimetres, administered to animals caused death with hypothermia.

Under normal conditions the colon bacillus constantly secretes in the alimentary canal poisons which are partly destroyed by the intestinal epithelium, partly arrested by the liver, and the excess contributes to the toxicity of the urine.

This is observed in quite a number of general diseases, even when the intestines are not involved, in which the colon bacillus becomes more active and produces a greater amount of toxic substances by virtue of organic disturbances.

Typhoid Fever.—The typhoid toxine has been studied by a great number of investigators, among whom it is convenient to cite especially Chantemesse and Widal, Sanarelli, Brieger, and Fraenkel.

Chantemesse utilizes a special medium: it is a cold maceration of spleen and bone marrow to which is added a small amount of human blood. The maximum of toxicity is observed from the fifth to the sixth day. Inoculated into animals, this toxine produces different effects according to the dosage: A large dose causes diarrhœa and produces death with hypothermia. With a weaker dose, the first phenomenon is a paroxysm of fever, and the animal succumbs by cachexia.

At the autopsy, abundant yellowish diarrhœal fluid is found in the intestines; the spleen is highly coloured. The urine is seldom albuminous.

Streptococcus.—Cultures of streptococcus, especially when protected from air, contain substances which exert a marked action upon the nervous system, bringing in its train rapid emaciation, paralyses, and death within two or three days. The active substance is precipitated by alcohol; it is partly destroyed by heat.

Staphylococcus.—Staphylococcus generates multiple toxic products, of which Rodet and Courmont have made an excellent study.

Its cultures contain a pyogenic substance precipitable by alcohol, and substances soluble in this liquid, which predispose to infection, and others which provoke a vaso-dilatation. The substances precipitable by alcohol provoke trembling, tetaniform convulsions, and produce death within a few hours. The substances soluble in alcohol produce anæsthesia and kill by arrest of the heart's action.

Glanders.—The soluble products of the bacillus of glanders, studied first by Finger, produce rapid death, or, if the dose be less strong, provoke paralyses and death by cachexia.

One of the most important properties of the sterilized cultures is that their injection causes a very notable rise of temperature in ani-

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mals affected with glanders. This result, discovered by Kalning, has been turned to use in practice. A lymph is prepared and frequently employed in veterinary medicine for the diagnosis of latent or suspected lesions.

Tuberculosis.—The action of glanders lymph may be compared to the action exercised by Koch's lymph or tuberculin. The injection of the latter is also followed by a reaction in tubercular subjects. But tuberculin, prepared by concentrating the cultures or by triturating the bacilli, does not represent the true soluble products—that is, the primary substances. Of the latter there are many. There are a hypothermizing toxalbumin; a ptomaine, which causes dyspnœa, hyperpyrexia, and produces death within two or three days; a toxalbumin, producing foci of necrosis at the site of injection; and a toxalbumose, which lowers the temperature of healthy animals and gives rise to congestive and febrile reactions in tubercular subjects. There also have been found in cultures or extracts prepared from the organs of tubercular animals substances the injection of which has been followed by a progressive emaciation. Besides the matters contained in the cultures, we must mention those encountered in the protoplasm of the bacilli; Koch has discovered therein a pyogenic substance. Prudden and Hodenpyl have shown that the dead bacilli possess the property of causing the formation of granulations similar to tubercles.

Toxines produced by Nonbacterial Infectious Agents

The investigation of toxines produced by infectious agents higher than bacteria has seldom been undertaken. This is due to the fact that most authors, persuaded that the bacteria have a monopoly of producing infections, have not attached sufficient importance to the problem. Those who have attempted experiments have generally arrived at negative conclusions.

It is to be remarked, first, that every parasite causing the development of a lesion secretes or contains a toxic substance; otherwise, it would have been perfectly endured by the tissues. This remark is applicable even to inanimate substances; they do not act unless they are soluble. On the other hand, the fact that toxines are absent from a culture bouillon does not warrant the conclusion that they are not produced in the living organism. In the case of a great number of pathogenic bacteria, in order to prove the presence of a toxine, it is necessary to utilize the most complex media and vary the procedures of sterilization. In ordinary bouillon, most bacilli produce no appreciable quantity of poisons.

When we see a parasite induce grave or fatal disorders, even when it remains localized at some point of the organism, we are forced to

admit that it has engendered some soluble product. In this respect nothing is more instructive than the history of *Oidium albicans*. This vegetable, inoculated beneath the skin or in the peritoneum, can produce nervous troubles—paralysis or movements of rotation around the longitudinal axis. The animals succumb within from three to fifteen days; the autopsy proves the absence of all visceral lesions, and that the parasite has not left the point where it was introduced. It is therefore impossible to explain the phenomena and death except by the absorption of some toxic matter.

In order to render the hypothesis incontrovertible, the poison must be discovered in the cultures. In injecting into rabbits cultures sterilized by heat, it is found that the more virulent the specimen employed the greater is the toxicity. With a less active parasite, 10 or 12 cubic centimetres will provoke no trouble whatever; with an intensified vegetable, 5 cubic centimetres will cause death. The dose is doubtless very high, if it be compared with the one which kills in cases of diphtheria or tetanus; but it is not greater than that which must be employed when the typhoid bacillus is used. Moreover, the parallelism existing between the increase in virulence and the toxicity is a good demonstration of the rôle played by the oidium poison in the production of the phenomena caused by the living cultures.

On the whole, it seems to us permissible to attribute a general bearing to the facts that have been observed, and to conclude that all infectious agents act by toxic substances. The latter are not, in most cases, sufficiently known from the chemical point of view. The results of experimentation have demonstrated their existence and plurality. The fact heretofore referred to, that the toxicity of the blood and the urine is augmented in the course of infectious diseases, is a further proof of the formation and importance of microbic poisons.

ACTION OF TOXINES. REACTION OF THE ORGANISM

The toxines, the origin of which we have briefly indicated, produce, as we have said, a local lesion, and, at the same time, may impregnate the entire economy.

Locally, they alter the cells with which they come in contact. If they be very energetic, they destroy them; if they be less active, they induce degenerations followed by reactionary phenomena. The portion of soluble substances that passes into the circulation will effect similar modifications in the rest of the organism. According to the activity of toxines, the cells of the organs and of the tissues will perish or present more or less profound degenerations.

We have thus far supposed that the organism was absolutely passive—that it did not interfere with the devolpment of the microbe any

more than an inert liquid would; in reality, the phenomena are much more complex.

When a microbe penetrates some point of the organism, it finds itself plunged into fluids endowed with a certan antiseptic power. This is what is designated as *germicidal action*. If the microbe is but slightly resistant, it will be completely destroyed; if it is more vigorous, it will be only weakened, and after a first defeat will gain the upper hand and begin to multiply. Then a new mode of defence sets in. The leucocytes contained in the blood do an incessant patrolling; they guard the integuments and mucous membranes, run to wherever there is the slightest abrasion, and even pass through the mucous membranes to penetrate into the cavities, there to exercise their rôle of protectors. Every microbe tending to invade an organism will then find itself in the presence of migrating cells, always ready to re-enforce the fixed cells and exercise a phagocytic rôle.

If the microbe is very virulent, its multiplication is scarcely hindered; it develops and secretes noxious substances. The cells nearest the microbic focus may perish; the others will present reactionary phenomena often ending in a proliferation, with a return to the embryonic state and in a reappearance of their phagocytic power. The local reactions thus result in the increase of one of the defensive measures of the organism.

At the same time the toxines which invade the organism by absorption modify the nutrition of the cells, and the latter begin to elaborate their products on a new plan. It is known that the humours of the organism represent the product of the cellular secretions; there is thus a production of substances useful to the organism, some as germicides, others as antitoxines.

The germicidal substances which exist in small amounts under normal conditions render the medium unfavourable to the microbe; they exercise on it five species of actions: (*a*) They destroy it; (*b*) hinder its evolution; (*c*) or at least modify its form; (*d*) disturb its functions; and (*e*) cause its attenuation.

The antitoxic substances are those which no longer act on the microbe, to lessen its pathogenic potency, but upon the animal organism, to strengthen its resistance. They impregnate the cells, and thus shield them against the influence of toxines. They act, then, in a complex manner, by a roundabout mechanism, and not, as was once supposed, by neutralizing the toxines as an acid neutralizes a base.

If these favourable secretions be not called into play too late, and if they be produced with energy, the course of the disease will be hindered or arrested. If, however, their appearance be tardy and their

quantity insufficient, the organism will succumb in spite of the development of a certain degree of bactericidal power.

The humoral modifications, the mechanism of which has just been indicated, bring about a weakening of the microbes and favour the protective action of the cells.

We have already stated that at the point where the microbe is introduced cellular proliferations occur; at the same time certain cells succumb; they then assume the nature of foreign bodies, excite the nervous system, and induce a vaso-dilatation at the invaded site through reflex action. The leucocytes, according to the process discovered by Cohnheim, leave the blood vessels and migrate to the affected region; they are attracted by the microbic products and cellular waste, which possess the property of so-called *positive chemiotaxis*. Then a struggle ensues between the cells and the microbes, the successive phases of which have been unveiled by Metchnikoff in a series of admirable investigations. The cells take up the microbes, incorporate them, and cause them to disappear by a process of intracellular digestion. This is what is designated as *phagocytosis*. Unfortunately, the phagocyte is not always the stronger; overcharged with microbes, it may perish, sometimes after having again entered into the circulation; the auxiliary of a while ago will then transport germs and serve to disseminate infection.

The fixed cells of the tissues may come to the assistance of the leucocytes; the round cells of the connective tissues, Ranvier's clasmatocytes, having returned to their embryonic form, and certain cells of the hepatic or renal parenchyma, and the vascular endothelium, exercise a similar phagocytic rôle.

It remains to view the cases in which the microbe invading the organism is endowed with extreme virulence. Here no struggle is possible. The microbe finds in the humours an excellent medium for its development; it increases, produces negative chemiotactic substances—that is, substances capable of repelling the leucocytes—and gives rise to toxines which overwhelm the economy. No defensive reaction whatever can occur.

It is quite certain that between these different modes of infection innumerable transitions exist. It is possible, nevertheless, to sum up the various events as follows:

1. Nonvirulent microbe: Destruction by fluids normally germicidal. No disturbance.

2. Slightly virulent microbe: Destruction commenced by the germicidal humours and completed by the phagocytes; local lesion without gravity.

3. Virulent microbe: Formation of local lesion not constant; im-

pregnation of the cells of the organism; cellular reaction resulting in the production of germicidal substances—i. e., increasing the resistance of the cells. The germs, overcome by the humours, are destroyed by the phagocytes attracted by the positive chemiotactic properties of microbic products and cellular waste.

4. Very virulent microbe: Defeat of the organism. Very little or no cellular reaction; little, if any, humoral modification. Phagocytes repelled by the microbic secretions, which are endowed with negative chemiotactic power.

We shall consider all these phenomena, especially when treating of inflammation, immunity, and vaccinations.

CHAPTER X

NERVOUS REACTIONS

Rôle of nervous reactions in physiology and in pathology—Local and general reactions: causes of their variations—The different varieties of nervous reactions: psychical, sensory, motor, vasomotor, nutritive reactions—Nervous fever—Nervous shock.

ALL vital acts are but reactions aroused by external agents. Certain reactions are produced at the very point where the stimulus acts; these Dr. Bouchard calls *autonomous elementary reactions*. Others, more complex, are caused by modifications in the nervous system; these are the reflex actions properly so called. Their points of departure are all the terminations of centripetal nerves—i. e., nerves of general, special, or visceral sensibility. They result in psychic, sensory, motor, vasomotor, secretory, and trophic modifications, which are produced either at the point of departure by a sort of reflection comparable to that of a shuttle, or ending in more or less distant and multiple points.

The stimulations which serve as starting points for nervous reactions are continual, though often unconscious; they are indispensable for the regular performance of vital actions; they maintain the nervous centres in activity. Even under normal conditions they present incessant variations. The modifications of the barometer and thermometer influence considerably our psychical and physical aptitudes. It is a fact of common observation that one has not the same ideas, feelings, and energy at different seasons, even at different hours of the day. Rainy weather or excessive heat diminishes muscular energy; fresh air, and notably sea air, increases our activity. On the other hand, psychic influences can modify considerably the state of our organism, and, conversely, the derangements of our organs reflect on our ideas. The slightest gastrointestinal disorder engenders sadness and melancholy. All these variations are yet of a normal order; they do not constitute sickness, but often predispose to it.

Local and General Reactions.—The results of nervous reactions should be studied, as already stated, both at the point of their departure and at a distance from it.

Locally, a stimulation is expressed, in certain cases, by an abrupt and unconscious movement. When a hot object is touched unwittingly, the finger is withdrawn often even before the painful sensation has been felt. In other instances, a vasomotor modification takes place. Under the influence of a cold application the vessels contract and the part becomes bloodless. In case of a hot application, the reverse takes place. Finally, if an irritating agent enters the tissues, the result is an active congestion followed by œdema and diapedesis.

Along with the local manifestations, which are all of a defensive character, modifications occur at distant points, sometimes at symmetrical points. Taking up an experiment of W. Edwards, Brown-Séquard and Tholozan demonstrated that if one hand is dipped in cold water the temperature of the other hand goes down. The effect is not due to a loss of heat, but to an homologous and symmetrical reflex action. In certain cases the phenomena are dissimilar; an equilibrium is produced between the peripheral and central circulation. In still other cases the manifestations are more complex; the section of a nerve may produce zones of anæsthesia or hyperæsthesia at points having no connection with the distribution of the sectioned nerve.

There remains a third group, which comprises the general reactions following a local disorder: these are chills, delirium, convulsions, syncope, fever, and nervous shock.

Conditions causing Variations in Nervous Reactions.—The phenomena of reaction vary in intensity according to their point of departure. They are the more marked as the region stimulated is the more richly supplied with nerves. If, for example, the snout of a rabbit is briskly dipped in cold water, a respiratory syncope results; if its hind legs are plunged in—that is, a region more extensive but less rich in nerve endings—no notable trouble is observed.

It is readily understood that the intensity of reactions increases as does the excitability of centripetal terminations; frictions, the application of sinapism, the action of heat, by flushing the skin, render the sensibility keener and the reactions more energetic; conversely, cooling and local anæsthetics, such as cocaine, diminish or suppress the effects of reaction. It must only be added that, under these various conditions, the phenomena are more complex than might be supposed. When the nerve terminations are modified, there are modified thereby the stimulations which maintain the tension of the nervous centres and their reactionary aptitude.

We may, in reality, act upon the centres by acting on the periphery. We may also directly act upon them, for instance, by means of sections which, by abolishing certain restraining influences, increase the responsive power of other parts. Likewise, under the direct influence of

heat or cold, the nervous centres become more or less apt to act. It is, however, the toxic substances that generally intervene: the bromides, opium, and chloral hydrate exercise a well-known sedative influence, while strychnine causes spinal excitability to so high a pitch that the slightest stimulation provokes violent tonic convulsions.

Alterations of the pathways of transmission are by no means less important. If they affect the centripetal paths the result is retardation or trouble in the perceptions and reactions. If the centrifugal paths are the seat of alterations, at times cramps or contractures, and at other times trembling and irregular or insufficient movements, are observed.

In other instances the organs in which the reflex action ends are altered and present very grave disorders under the influence of the slightest peripheral stimulation. The most striking example is offered by cardiac pathology: a slight impression, which provokes simply some palpitation in a healthy man, may in a person affected by myocarditis or aortic insufficiency give rise to a fatal syncope.

Even in the normal state, nervous responses vary with a great number of predisposing conditions, which we must now rapidly pass in review.

It is, in the first place, the influence of the species. The higher the being, the more energetic are the reactions. Stimulations that elicit no response in animals may cause accidents in man: a violent blow on the testicles is well endured by a dog; in man it not infrequently causes a lipothymia or a syncope. The nervous shock is likewise rare in animals, or occurs only under the influence of exceedingly violent causes.

To confine ourselves to the human species, we shall first note the influence of sex. In women, nervous reactions are far more easily called forth than in men; women blush or grow pale, laugh or cry, on the slightest pretext. In order, however, to fully appreciate the differences, we must consider the genital period. In young children the nervous system is always of a feminine character; it is a matter of common observation that with them reactions are quick, mobile, and excessive. At an advanced age sexual differences become less marked: from a physiological as well as a psychical standpoint the old man is a being who reacts little; the strongest impressions leave him almost indifferent. Likewise, when an infectious disease breaks out, the reactions, so tumultuous in the child, so marked in the adult, are hardly noticeable in the aged, and we are greatly surprised, at the autopsy, to find, for instance, a pneumonia arrived at the stage of gray hepatization without its existence having been revealed by any symptom whatever.

Age and sex differences aside, there are numerous factors which intervene to impress the nervous system with special reactionary aptitudes, and thus confer on the individual a personality. The most important are the hereditary and inborn influences.

Psychical characteristics and reactionary tendencies are transmitted from parents to children. Of this we shall treat at length in the following chapters. All the children of the same family are not absolutely alike; their responsive aptitudes are often very different, because the state of the nervous system in the parents has not been the same at the different periods of life. The nervous system of a child reproduces the nervous systems of the parents, such as they were at the epoch at which conception took place.

In general, children born of young parents are more apt to react; they are more lively and more cheerful. But when the generators are older, and have experienced disappointments and disillusions which are almost unavoidable, and their nervous systems have undergone the shocks of external events and they have acquired that sort of sadness which characterizes mature age, then the child comes to the world calmer; it will not have the illusions and enthusiasms of those born before it; it will often be inclined to melancholy. If conception is still more tardy, the child will be recognised by its lack of youthfulness, its precocious senility, which seems to continue the senility of its parents.

In the next place, the state of mind, the physical and psychical conditions that existed at the moment of conception or during gestation must be noted. In these cases the influence of the father is naturally less marked, as it acts only during the period of formation of the spermatozoids; while the mother's influence makes itself felt alike during the development of the ovum and the entire duration of pregnancy. It even seems that the disturbances of infectious or neuropathic origin occurring during gestation have a far greater influence on the product than those existing at the moment of conception.

The incessant modifications transmitted by heredity explain the development of races and the influence of civilization. The effect of the latter is to diminish the intensity and fatality of nervous reactions. It can be said of the savage what Virchow said of the child: he is a medullary being. In the civilized adult the brain is predominant and rules the subjacent centres; thus is created the will which becomes capable of arresting various reactions, even the vasomotor reactions; it becomes possible to refrain from crying under the influence of pain, and from flushing or getting pale under the influence of emotion. It happens, however, that at a certain moment the will, even the most energetic, undergoes more or less lengthened eclipses. In the course of diseases or during convalescence the highest psychical manifesta-

tions are weakened, and, consequently, nervous reactions assume that character of fatality which they seemed to have lost in the superior races.

Nature of Nervous Reactions

Psychical Reactions.—In their highest manifestations nervous reactions are expressed by phenomena of an intellectual order. We have already established that all ideas have an external origin. According to the old adage, so passionately criticised by the spiritualist school, it can still be maintained that all our present acquisitions have originated from sensitive and sensorial impressions. But while rejecting the existence of innate ideas, we must recognise that the human brain presents from birth certain special aptitudes. We inherit, to a certain extent, the experience acquired by our parents. It is quite certain that the brain of a child born of civilized parents must not have the same intellectual predispositions as the brain of one born of savage parents, and it is hardly probable that the son of the primitive man, if he were possibly transported into our world, would be able to acquire the knowledge inculcated in the children of our epoch.

The intellectual and moral properties thus developed in races and families may become perverted in a great number of diseases. At the present day we no longer question the influence of the body on the mind. It is a commonplace truth that character, intelligence, and capacity for work are considerably modified in the course of most diverse diseases. The sadness and hypochondriasis of individuals suffering from gastric, intestinal, hepatic, or genito-urinary affections and the delirium incident to febrile diseases are facts so open to common observation that we do not need to dwell on them. Reciprocally, psychical impressions modify our bodily state. Emotion provokes polyuria or diarrhœa and arrests digestion. It even suffices that the mind should fix itself on an idea in order that there be produced a series of almost imperceptible movements which are but a tendency to the act. Hence by perception of such abortive movements the possibility for those endowed with a very keen tactile sensibility to read thoughts.

Sensory Reactions.—Reactionary manifestations often affect the sensibility. A nervous excitation may produce anæsthetic or hyperæsthetic phenomena: a superficial pain cures a profound pain. Brown-Séquard has shown that the projection of a current of carbonic acid on the larynx is followed by a cutaneous anæsthesia. In a subject with a predisposed nervous system, for instance an hysterical woman, even a slight traumatism may give rise to a sensitivo-sensorial hemianæsthesia—viz., to abolition of general and special sensibilities on one side of the body.

Motor Reactions.—Reactions occurring in the motor sphere are far more numerous. The best example is afforded by the tickling of the sole of the foot. At first, the leg is abruptly withdrawn, even in sleep; this is the plantar reflex. If the stimulation be kept up, the individual raises both feet: then a nervous rictus, spasms, and, finally, convulsions follow. If a more sensitive person is operated upon, convulsions appear far more readily. With children the slightest irritation is enough—a fish bone fixed in the tonsil, an intestinal worm, and the pain of teething are familiar causes.

Considering the same influences in an hysterical person, it must be noted that the most trifling excitement may call forth grave manifestations. A slight shock may give rise to paralysis, trembling, or contracture. These various symptoms do not appear at once; response is slow; the individual must muse on his accident, and induce, so to say, self-suggestion in order that morbid manifestations be aroused.

In certain cases the frequent repetition of the same act is followed by contractures called functional cramps; such are the cramps of writers, telegraphers, and pianists that are observed in individuals predisposed by some nervous taint.

Excitations also give rise to inhibitory phenomena, which are to be well distinguished from paralytic manifestations. Inhibition is an active phenomenon. For instance, the stimulation of the pneumogastric nerve causes arrest of the heart through inhibition. In medicine we often see a violent stimulation to determine an arrest of circulatory or respiratory movements, or, as is commonly said, a circulatory or respiratory syncope. In the same order of ideas we may mention the impossibility of motion experienced by individuals when under the influence of a violent emotion. At a higher degree—that is, in a predisposed subject—an attack of catalepsy occurs.

Vasomotor Reactions.—Another group of nervous responses is constituted by vasomotor reactions. Every stimulation, especially if painful, determines a vaso-constriction, even when the subject is anæsthetized. Vasomotor modifications are observed every moment in physiology as in pathology. We need barely mention the well-known influence of heat and cold. In the case of a chemical agent a congestion is produced, followed by an exudation, which dilutes or neutralizes the noxious substance. But it is in the struggle against infectious agents that the rôle of vasomotor responses intervenes most efficiently; the active congestion permits diapedesis, and thereby phagocytosis.

When a vasomotor modification takes place at one point of the economy, others are generally produced in more or less distant parts. An equilibration is often admitted between the superficial and the profound circulations, and it is upon this idea that revulsive medica-

tion is based: dry cupping, by drawing the blood toward the skin, is supposed to relieve the congestion of the subjacent parts. The facts are real, but they are more complex than was formerly believed. In some instances the variations occur in the same direction; thus, the application of the ice bag to the cranium excites the vaso-constriction of the meningeal vessels. Frédéricq, who has proved the fact experimentally, remarks that the phenomenon is produced too quickly to be attributed to a reduction of heat; it is a manifestation of a nervous order. Similar phenomena must occur in many cases, and it is probable that an attack of cold that gives rise to pneumonia must act by first producing a vaso-constriction of the pulmonary blood vessels. The congestion revealed by clinical examination represents already a phenomenon of reaction.

Under the influence of a unilateral stimulation, symmetrical vaso-motor responses are often produced, whether of the same or of a contrary kind. Thus, if one hand is exposed to cold, the other also grows cold. On the contrary, congestion of one of the kidneys induces anæmia in the other; extirpation of the superior cervical gland of the sympathetic, which produces vaso-dilatation in the enervated ear, determines vaso-constriction in the intact ear.

In a great number of instances circulatory disturbances have their starting point in some distant organ. Stimulation of the biliary passages, as is realized by lithiasis, produces in the lungs vaso-constriction, followed secondarily by congestion. It is a reflex action following the sympathetic both as a centripetal and a centrifugal path.

If the phenomena are very intense, the vessels overfilled with blood may burst. A cold bath has been able to produce cerebral hemorrhage, anger has been followed by epistaxis. Cerebral lesions are capable of producing subpericardiac and subpleural ecchymoses, or even veritable foci of pulmonary apoplexy.

Vasomotor disturbances often terminate in the production of œdema. It is demonstrated that venous obstructions are generally insufficient to permit serous transudation; there must be, in addition, some vasomotor trouble. If the three veins of the base of the ear of a rabbit be tied, no disturbance is observed; but if we then extirpate the upper cervical gland of the sympathetic, œdema of the pavilion is produced.

The vasomotor disturbance so decidedly represents the principal factor that, under certain pathological circumstances, it suffices to give rise to œdema. It is thus that a whole series of cutaneous manifestations develops, especially urticaria and fluxions, which, in arthritics, are observed in the eyelids in consequence of a cold draught. Under similar circumstances arise also the pseudo-lipomata of rheumatics.

Secretory Reactions.—Whether there be or not any vasomotor modification, the nervous system may call into action the glandular secretions. We have already referred to emotional polyuria and diarrhœa; we shall add the sweats, and notably the cold perspirations, which represent the most remarkable example of dissociation between secretory and vasomotor phenomena. In other cases, the sweats, far from being increased, diminish or are suppressed: a violent emotion produces dryness in the throat; a blow upon the abdomen or a crisis of hepatic colic gives rise to a transitory anuria. It may be stated that, as a rule, slight stimulations increase the secretions and that violent stimulations diminish them. This can be experimentally demonstrated by stimulating more or less the sciatic nerve. Neuralgia of this same nerve gives similar clinical results: if of moderate intensity, it increases diuresis; if violent, it gives rise to oliguria.

Nutritive Reactions.—One of the most interesting functions of the nervous system consists in regulating the movements of nutrition. Its influence upon the carbohydrates has been easily recognised. An emotion produces a transitory glycosuria in certain individuals; but if the unhealthful excitations be repeated, glycosuria becomes permanent: a nervous diabetes develops.

Similar modifications occur in nitrogenous substances. There are albuminurias caused by nervous reactions; they occur as the result of cutaneous stimulations—for instance, when an individual suffering with psoriasis scratches himself. They are observed also in consequence of strong psychical emotions. At other times the disturbance in the elaboration of nitrogenous substances is expressed by modifications in the urea. This result has been turned to account by therapeutists: in order to increase the production of urea, cutaneous frictions with horsehair gloves, douches, or a sojourn on the seashore are prescribed. Analysis of the urine demonstrates that sea air increases by 3 grammes daily the excretion of urea; sea bathing produces an increase of 1 gramme, and a bath in hot sea water 2 grammes. In all cases cutaneous stimulation favours oxidation.

Likewise, it has been demonstrated that pleasant impressions, joy, happiness, raise the quantity of urea. Böcker has seen an individual lose, under the influence of a great joy, 1,159 grammes of his weight and eliminate through his urine 40 grammes of urea in twenty-four hours. This loss, which expresses an increase in nutritive exchanges, is followed by an increase of appetite and an energetic reparation. On the other hand, depressing causes, sad news, diminish oxidation and hinder assimilation; the sensation of hunger grows less lively and emaciation makes rapid progress. In certain instances nervous stimulation, whether physical or psychical, a blow upon the

head or an emotion, may engender a permanent disorder of nutrition—viz., azoturic diabetes.

Although the fact is not demonstrated, it is probable that the nervous system intervenes in the elaboration of uric acid, and, consequently, in the pathogenesis of gout, since fatigue, excesses, and anxieties play an important part in the causation of the disease.

The trophic influence of the nervous system accounts for certain disturbances which one might at first be tempted to explain by another mechanism. Thus, articular lesions are followed by atrophy of the muscles subjacent to the diseased joint. The phenomenon is not due to the immobility of the member, but to a true reflex. By severing the posterior roots in a dog, Raymond and Deroche found that the traumatism of the knee did not produce amyotrophy: they had suppressed the centripetal portion of the reflex arch.

Trophic disturbances may also be responsible for pigmentary phenomena. Many a dyschromia is due to some nervous influence. The most curious instance is that recorded by Gubler: In a man suffering from trifacial neuralgia the hair grew without colour during the crisis, so that after a certain number of attacks it presented a zebralike appearance.

By controlling nutrition, the nervous system also regulates the temperature. There are nervous fevers, of which hysterical fever is the most familiar type.

When an individual is weakened by any cause whatever, and particularly by a disease, the slightest excitement produces fever. Annoyance raises the temperature of the sick; when patients hate to take cold baths, it is often observed that, after a forced immersion, the thermometer rises a few tenths of a degree, despite the loss of bodily heat. It is a familiar fact in hospitals that the temperature of the patients increases on visiting days. In the convalescents it slightly rises when they are permitted to make their own toilet or to read.

Reciprocally, nervous reactions may cause a diminution of temperature. This is at least what occurs under the influence of violent impressions, which often give rise at the same time to a series of manifestations collectively called nervous shock.

Nervous Shock.—*Nervous shock* is essentially characterized, from a pathologico-physiological standpoint, by arrest of exchanges between the cells and the plasmas (Brown-Séquard); in other words, it is an arrest, or rather a diminution, of nutritive activity occurring through reflex action, under the influence of a sudden and violent excitation. It is an active phenomenon, and not the result of nervous exhaustion. So it is readily understood that shock should be more frequent in men than in women, and in adults than in the young and the aged. It is to

be noted, however, that when it is produced in the aged it assumes a character of exceptional gravity.

Nervous overexcitement is favourable to the production of shock; during the Commune of Paris shock was far more frequently observed among the insurgents than the regular troops. On the other hand, nervous exhaustion is unfavourable to its development; hence a first shock is not aggravated by a fresh excitement. A grievously wounded man listens with indifference to the announcement of a catastrophe; it would not be so if shock, as is often said, were due to nervous exhaustion.

Among the causes of shock, great traumatisms must be put on the first line, then violent excitations of the cutaneous nerve terminations. Whether an immersion be made in boiling or cold liquids, the effect, from this point of view is the same. We shall not advert to this question, already referred to on page 43. We have likewise pointed out that sideration by electrical currents (page 58) belongs to the same order of phenomena.

In the case of localized stimulation, the effects vary with the regions; they are the more marked as the part is the more richly supplied with nerves and more sensitive. It is not, however, the external parts alone than can be the starting point of nervous shock; hepatic or renal calculi, the colic of intestinal occlusion, and pulmonary or cerebral emboli can produce the same effects: these are veritable *internal traumatisms*.

Excitation may also be produced by chemical substances, and especially by irritating vapours, acting upon the larynx and lungs. Thus, chloroform, the effects of which are, of course, complex, may, by stimulating the terminations of the laryngeal nerves, give rise to a series of inhibitory acts—namely, cardiac syncope, respiratory syncope, and arrest of nutritive exchanges.

The last, but not the least, of causes of nervous shock must not be overlooked—viz., moral impressions. It is well known that Sophocles, Denys the tyrant, and Pitt succumbed to the sudden announcement of some startling news. A great joy or a great fright may cause sudden death, or the series of phenomena that characterizes shock.

An individual suffering with this syndrom, a man, for instance, who is the victim of a grave traumatism (such is most frequently the case), is in a state of complete prostration. He is lying down, motionless, absolutely indifferent to all his environment and often altogether unconscious; the skin is pale, covered with a cold, clammy sweat, the mucous membranes are bloodless, and the eyes half closed. When his eyelids are raised the pupils are found to be dilated. Sensation is extinct, respiration irregular, pulse slow, irregular, and weak; the veins

contain but a small amount of blood, which presents a bright colour. Peripheral and central temperature goes down; the thermometer placed in the rectum does not rise above 36° C. Death thus supervenes in adynamia and collapse. In grave cases, fatal termination occurs within a period varying from thirty minutes to twenty-four hours. When the evolution is to be favourable, the symptoms gradually disappear, but they sometimes leave as sequels various nervous disorders: disquietude, agitation, neurasthenia, and paralysis. Such cases are observed especially in consequence of railroad accidents.

The explanation of these various phenomena is already pointed out by the analysis of the symptoms. The modifications of circulation and respiration, and the red colour of the venous blood, which, as the analyses made by d'Arsonval have shown, contains very little carbonic acid, sufficiently demonstrate the profound disturbance of nutrition. Cellular life is suspended and modified. The recent researches of Philippen established the fact that during shock a veritable auto-intoxication is produced as the result of disorders occurring in cellular nutrition. The toxic substances thus generated can not pass from the cells into the blood, and, on the other hand, toxic products no longer pass from the blood into the cells. The most active poisons can be introduced into the organism with impunity. It has been experimentally demonstrated that animals in a state of shock do not respond either to strychnine or veratrine; and clinical experience establishes that it is in slight cases alone that alcohol causes semi-intoxication and opium induces sleep.

CHAPTER XI

DISTURBANCES OF NUTRITION

The two characteristic phenomena of nutrition: assimilation and disassimilation—
  Cellular nutrition: the six acts to assure it in the higher beings—Disturbances
  of nutrition—Starvation—Disturbances of digestion and absorption—Varia-
  tions of cellular nutrition in physiological and pathological conditions—
  Diatheses.

Nutrition is the principal property of living matter: it essen-
tially characterizes life.

It comprises two orders of phenomena: assimilation and disassimi-
lation.

Assimilation is represented by a phenomenon of organic synthesis.
The cell seizes upon the nutritive materials placed at its disposal,
and groups them together in such a manner as to form a very complex,
and therefore very unstable, molecule. In order that these phenomena
may be produced, a certain amount of force must be absorbed—i. e.,
pass into a state of latency.

Then comes the second phenomenon, *disassimilation*. The formed
molecule disaggregates and is reduced to simpler and, consequently,
more stable elements; at the same time a certain quantity of energy is
liberated. Molecular destruction is thus attended with a disengage-
ment of force; the wearing out of the cell results in the manifestation
of life. Thus goes on the process of a continual construction and de-
struction, and thereby an incessant renovation.

The substances of disassimilation have become useless. They are
even harmful, for the cell does not reject them such as it has absorbed
them; it abandons them in an altered state, unfit for its nutrition.
They can, however, be utilized by other beings, who will cause them to
undergo new transformations, and bring them back to their first state.
So there is a real circulation of matter, which passes from being to
being and returns to its point of departure.

To take a concrete example, let us consider how animals and plants
live. Of course, cellular life is alike in both cases. As Claude Bernard

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has shown, there is not a vegetable physiology and an animal physiology. The laws of nutrition are the same: the plant cell liberates force, as does the animal cell, and, like it, produces then carbonic acid. But the plant spends much less energy, and the phenomena predominant in it are those of assimilation. It seizes upon carbonic acid and unites it to water under the influence of solar rays, thus reconstituting a hydrate of carbon, which furnishes the animal with vital force. It is, then, the sun that, through the plant, furnishes the necessary energy; the solar rays, as Herschell has pointed out, are the true cause of all nutritive phenomena and the source of all vital energy.

When a living being is placed in a confined space, there comes a moment when the vital manifestations cease. It is not because the aliments are exhausted, for these can be supplied without restoring life; the vital arrest is due to an accumulation of useless matter—namely, to *auto-intoxication*. The being has poisoned itself by its own products. Let these be artificially eliminated, and life will continue; let another being of a different nature, capable of turning to use the cellular wastes, be introduced into the same space, life will be resumed, and, in this manner, there will be realized what takes place in Nature.

If we consider the life of the unicellular being, we see that nutrition is characterized by four series of phenomena: A physical phenomenon, endosmose, by which nutritive substances pass from the exterior to the interior of the cell; a chemical phenomenon, assimilation, characterized by an organic synthesis and the storing up of force; another chemical phenomenon, the reverse of the preceding one, disassimilation, accompanied by a disengagement of accumulated energy; finally, a physical phenomenon, exosmose, by which the matter which has become useless or harmful is thrown out of the cell. In order that endosmose and exosmose may be produced, the nutritive substances must be in a state of solution. We can conclude, therefore, that to a unicellular being life is possible only in a liquid medium.

The same is true of the higher beings, so far at least as cellular life is concerned. An artifice permits life out of water; that is, the creation of an internal medium—blood, lymph, plasma—whence the cells draw the elements of their nutrition. In physiology, as in chemistry, active manifestations can not take place unless the substances are dissolved.

Aerial existence presents a new complication. In order that nutritive materials may reach the medium, and that the products of disassimilation may be eliminated, it is indispensable that there should exist a certain number of organs. Thus the phenomena of nutrition become complicated. New functions are added; some for the

entrance of alimentary substances, others for the rejection of waste products.

We are thus led to admit six successive acts in the nutrition of higher beings:

1. Transmission of food by the digestive canal; transformation of aliments by the juices flowing into the gastrointestinal tract. The effect of these transformations is to hydrate the substances in order to render them dialyzable; the starch is saccharified, the albumins are peptonized, the fats are partly emulsified and partly decomposed into fatty acids and glycerine.

2. Absorption. The dialyzable substance passes through the intestinal walls. But the phenomena are not merely of a physical order; there is, at least in some measure, a vital process, in which the epithelial cells of the intestine take an active part.

3. Dehydration of the aliments that have been hydrated in the gastrointestinal cavity. Had the aliments preserved the power of diffusion acquired in the intestine, they would be eliminated as fast as they were introduced; they undergo, therefore, a process of dehydration, which, rendering them less readily dialyzable, adapts them either for nourishment or to be stored up in certain parts where they form reserves. Dehydration begins in the intestinal walls, where peptones form new albumins and the decomposed fats are combined anew; it is finished in the lymphatic glands, and especially in the liver, which arrests the fatty acids, the peptones, and the sugar. Glucose is dehydrated and forms a matter analogous to starch—namely, glycogen—which accumulates in great quantities in various tissues, in the muscles, and chiefly in the liver.

4. Nutrition of cells, comprising the four acts above indicated in reference to unicellular beings. Only, it is not in the ambient medium but in the interstitial plasma that the cells appropriate the matter they want, and eject the waste substances. The latter pass into the blood and are eliminated. But, in order to easily leave the organism, they must become dialyzable.

5. Transformation of the products of disassimilation, which become dialyzable. The liver plays here a very important part; it is in its parenchyma that nitrogenous products undergo the ultimate transformation which reduces them to the state of urea, a crystallizable body, which readily leaves the organism, and even acts as a diuretic; it favours the renal emunction.

6. Rejection of the useless substances by the emunctories, chiefly by the lungs and kidneys, and next by the skin and the various glands with secretory ducts.

It is possible, then, to find out, at least approximately, the nutritive

state of a man by examining his excreta. It has thus been established that an adult voids in twenty-four hours 250 grammes of carbon and 18 grammes of nitrogen; he must ingest, therefore, each day, aliments that will furnish the same quantities of these two substances. He will obtain the 18 grammes of nitrogen by consuming 500 grammes of meat, but for the 250 grammes of carbon he will need 2 kilogrammes of meat. These figures show the necessity of a mixed alimentation. If vegetables are added to the diet, the ration of maintenance is obtained by giving 5 parts of carbohydrates for 1 part of nitrogenous matters. When these conditions are not fulfilled, disturbances break out. To understand the mechanism, we must first consider what happens in case of absolute inanition.

Starvation.—When a being is deprived of nourishment, of the two acts characterizing cellular nutrition, only one is preserved; disassimilation continues, and death supervenes when the body has lost about 40 per cent of its weight. All the tissues do not equally take part in the emaciation. Fat diminishes in the proportion of 97 per cent. The viscera are affected in the following order: First, the spleen, and then the liver, the muscles, the kidneys; the most resistant of all are the heart and the nerve centres. Their loss does not exceed 3 per cent of the initial weight. These various results are easily explained. At the beginning of starvation, the sufferer consumes the fat; when this is exhausted, he resorts to the nitrogenous substances. At this moment, urea increases in the urine, albuminuria sets in, the organic temperature falls, and then the situation becomes grave.

Survival varies considerably, according as one takes or suppresses liquids. A dog deprived of nourishment and of beverages succumbs in twenty days; a dog deprived of food, but having water at its disposal, is still living at the end of thirty days, and, if fasting ceases, it may recover health. The same differences are observed in the case of man, and the celebrated fasters of recent years have always been careful to continue drinking. Water is beneficial because it washes the organism and carries off the products of disassimilation; it prevents auto-intoxication.

Man is seldom submitted to absolute fasting; there is generally an insufficiency of nourishment and a bad quality of food. This is what happened during the great famines which ravaged Europe in the Middle Ages and until the eighteenth century; that is also what occurs during wars in besieged towns. On such occasions a whole series of disturbances is observed, mostly due to the secondary action of infectious germs. Bad nourishment weakens the organic resistance and leads to the development of epidemic diseases, markedly of typhus.

Likewise, in clinics, those who are ill nourished, either in conse-

quence of poverty or some organic lesion (a stricture of the esophagus or the pylorus), present a series of symptoms, some of which are the direct result of starvation, others are due to superadded infections, owing to the weakness of the organism. Among the former we shall indicate emaciation, anæmia, dropsy, and cardiac and cerebral disorders, notably delirium; among the latter, cutaneous eschars, pulmonary gangrene, blood infections, and especially tuberculosis.

Nutritive Disturbances due to Disorders of Digestion.—For the study of the disturbances of nutrition, we shall review in succession the different acts which follow one another in the higher beings. It is first, as already stated, the action of the digestive juices which hydrate the ingesta. When the aliments are too abundant or of bad quality, when they are indigestible or not appropriate to the age, very complex disturbances result. The nondigested food falls an easy prey to the microbes swarming in the alimentary canal; the result is an increase in intestinal fermentation, catarrh, or inflammation of the digestive tube, and dilatation of its various parts, markedly of the stomach and large intestine. From a functional point of view, an attack of indigestion, dyspepsia, sometimes lientery, follows. The subject gets thin, nervous manifestations appear, various tissues are disturbed in the nutrition, and often nodes develop around the second phalanges (*nodosités de Bouchard*).

At other times, it is the case of those who take in excess some particular kind of food; some, for instance, abuse the carbohydrates: a too great amount of glucose is absorbed. The cells are unable to utilize all, and some of it passes into the urine; thus is produced a first variety of alimentary glycosuria. In other instances the nitrogenous substances are too abundant; they are absorbed, but do not undergo their complete circle of evolution; they stop at the stage which precedes the formation of urea. According to certain authors, uric acid is found in excess, and may pass into the urine or accumulate in various parts of the organism, thus giving rise, at least in some cases, to the affection called gout.

We have already pointed out that the second act of nutrition could not be explained by the laws of physics alone, that a large part is due to the vital action of the epithelium and membranes of the intestine. The peptone, for example, becomes dehydrated while passing through the intestinal walls, so that none of it is ever found in the blood, not even in the portal vein. Under certain pathological conditions it no longer undergoes its transformation into albumin; it passes into the system, and, as it is no longer good for nutrition, it is found in the urine. In this manner is created the peptonuria of intestinal origin— the enterogen peptonuria of the German authorities.

Once absorbed, nutritive substances undergo a final transformation in the mesenteric glands and the liver. Physiology has not taught us much respecting the function of the lymphatic glands, nor does pathology tell us anything about disturbances dependent upon their alterations. We are better informed as to the fate of all the substances which enter by the portal vein. The liver stops the traces of peptone which may have escaped the dehydrating action of the intestine, and it modifies the albumins that are not yet quite fitted for the renovation of the cells. No wonder, then, that there exist, in liver diseases, at one time peptonuria (hepatogenic peptonuria), at another albuminuria. It is especially on the ternary substances that the liver exerts its action. It arrests the sugar which the portal vein contains in excess after meals; it dehydrates and stores it up under the form of glycogen, which it transforms into a new sugar, somewhat different from the ordinary glucose, and which it diffuses according to the needs of the organism.

If the liver is altered, the sugar is not arrested; it passes into the blood and is eliminated by the urine. This glycosuria also is produced after meals; it is an *alimentary glycosuria* due to hepatic insufficiency.

Variation of Cellular Nutrition under Physiological Conditions.— The variations of cellular nutrition are exceedingly numerous, *even in the normal state*. There exists, nevertheless, a medium type of nutrition, which is modified, however, according to age.

During the first years of life, assimilation predominates over disassimilation; the child accumulates matter; it constructs, so to speak, its cells.

If the alimentation of the infant is bad or insufficient or too copious, gastroenteritis occurs, the stools become green and acid, they provoke erythema of the buttocks, vulva, thighs, and even the heels. The child loses flesh, and has the aspect of a little old man; the skin loses its elasticity, and at the same time the abdomen grows large, the liver becomes hypertrophic, the scanty buccal secretion permits the development of various germs, and aphtha makes its appearance. Such are the disturbances described by Parrot, in so striking a manner, under the name *athrepsia*.

In other cases a defective ossification and rachitis are the result.

In some instances the phenomena are different, either because the digestive disorders are not identical, or because the child is born with a special inheritance, or because the evil effects of a vicious alimentation are aggravated by lack of oxygen and the sun; at all events, the child becomes lymphatic or scrofulous.

At the moment of puberty other disturbances are imminent. At

this period a profound modification in general nutrition takes place; if the individual is predisposed by a bad inheritance, if his organism is weakened by overexertion, if reparation is insufficient, then a general affection—chlorosis—develops.

Various hypotheses have been put forth concerning the pathogenesis of chlorosis. Referred by some to lesions of the vascular system, by others to genital disorders, by others to digestive perturbations, and described as a blood disease, chlorosis is most frequently observed in children born of tainted parents. Tuberculosis is found in the antecedents of three fourths of the patients. It is probable that the disorder transmitted by heredity strikes the hematopoietic organs, and hinders them from providing for the nutrition required by the additional activity. Hence, chlorosis is particularly frequent among the young girls of the labouring class who are forced to do too much fatiguing work. In the male it is met with, on the contrary, as Dr. Hayen has pointed out, among the higher classes, the influence of cerebral exertion being, in fact, more detrimental than that of manual toil, for which man has a greater aptitude.

We must not, however, deny the part which menstruation may play in the genesis of disturbances observed in young girls at puberty. At each menstrual period nutritive modifications occur, predisposing to disease. The urine contains more urates, the breath and sweat exhale a rather strong odour, which is due to an exaggerated production of volatile fatty acids. The nervous system, which intervenes so frequently in the production of nutritive disturbances, may also play a part in the development of chlorosis. Not infrequently this particular anæmia establishes itself suddenly, or at least in a few days, after a strong moral impression—a great fright or a violent sorrow.

Woman's nutrition is also modified during pregnancy and lactation. This is proved by the examination of the urine. With pregnant women the cellular wastes are more abundant than normally, and, if oxidation be insufficient, organic depuration becomes incomplete. This is explained by the frequent appearance of hepatic disorders, the production of albuminuria and peptonuria, and the variations in blood and urine toxicity. According to Bunge, important modifications occur in the distribution of the iron, previously stored up in the liver, where it formed provision for the development of the new being.

We have already noted that during childhood assimilation predominates over disassimilation. In the adult, the two acts of nutrition balance one another; in old age, disassimilation becomes preponderant; the cells are no longer capable of assimilation; the cellular tissue, the skin, the organs, the skeleton itself, gradually atrophy; the integument loses its elasticity, the osseous substance rarefies and be-

comes porous; hence fractures are easy, and may occur almost without cause. This decrease of nutrition predisposes the aged person to chilliness; moreover, it reduces his activity and energy and brings on both physical and psychical indifference.

Variations of Nutrition under Pathological Conditions.—Along with the modifications occurring under normal conditions, we must place those observed in pathology.

Nutrition may be accelerated, sluggish, or perverted. Setting aside the digestive disturbances already spoken of, we shall first consider the influence of the nervous system. We have cited many examples establishing the fact that general nutrition is profoundly modified through the nervous system. For the maintenance of its regularity, the continual influence of air and light on our skin is necessary; it is therefore disturbed when we live in a confined atmosphere, in badly ventilated or dark lodgings. It is not any less influenced by all causes affecting the nervous system. We have already pointed out the great importance, in this respect, of joy and sorrow, of activity and idleness. Where the influence of the nervous system upon nutrition appears most clearly is in the course of neuroses. In paralysis agitans, in neurasthenia, the nutritive disorder is expressed by an exaggerated excretion of phosphates. This phenomenon is most remarkable in hysteria. The amount of urea may fall to 2 grammes in twenty-four hours, and even to 75 centigrammes. There is, then, an almost absolute arrest of nutrition; hence it is that some hysterical women can refuse all nourishment without getting thin in a noticeable degree.

In some cases modification in the elimination of phosphates is observed. It is after an attack of hysteria that a very curious phenomenon takes place, discovered by Gilles de la Tourette and Cathelineau. We know that phosphoric acid is eliminated, being united to calcium and magnesium (earthy phosphates), to sodium and potassium (alkaline phosphates). Under normal conditions the proportion of the earthy to the alkaline phosphates is as one to three; after an attack of hysteria the earthy phosphates increase and correspond to half of the combined phosphoric acid. Such is the phenomenon constituting a reversion of the formula of phosphates.

Nutritive modifications may be produced by toxic substances, acting on the cells directly, or indirectly through the nervous system. Certain medicines, like iodide of potassium, excite disassimilation. Others, bromide of potassium, for instance, check it.

Taken in large and long-continued doses, morphine produces emaciation; under the same conditions, alcohol gives rise to obesity.

Among the substances that produce the most curious effects, lead must be mentioned, which disturbs the metamorphosis of nitrogenous

constituents, determines an accumulation of uric acid, and sometimes gives rise to gout (saturnine gout).

We know that the microbes act by the poisons they secrete; no wonder, then, that infections should provoke numerous nutritive disturbances. To be convinced of this, it will suffice to remember the profound emaciation of the patients. It is, however, the study of the excreta that furnishes the demonstrative information. Carbonic acid is exhaled in greater quantity, the urine contains an excess of extractive matters; urea decreases, at least in its proportion to the total of nitrogen; it is, in fact, replaced by less oxidized substances, by amido acids, and even by ammonia. In certain cases, however, cellular wastes remain stored up in the economy, and are rejected only at the moment of convalescence; it is under these circumstances that emaciation is mostly produced after the termination of the disease.

But we have already stated that all modifications occurring in the organism are almost invariably followed by reverse actions. When infection is terminated, repair begins and often becomes more active than disassimilation had been; hence the notable fattening so frequently observed. The fact is of common occurrence after typhoid fever. Likewise, consumptives, when they are cured, become obese.

It is well to mention, finally, that under the influence of microbic toxines humoral modifications are produced in the organism; germicidal and antitoxic substances are formed. All these changes must be attributed to a nutritive modification; the cells influenced by the microbic products react in a new fashion and modify the chemical constitution of the humours.

It is possible at the present day to ally neoplastic with the infectious process. The influence of tumours upon nutrition is undeniable, as is evidenced by the emaciation, which is so marked and rapid. It appears even particularly to affect the transformation of nitrogenous substances. Rommelaere has insisted upon the diminution of urea, which can not be accounted for merely by starvation. His assertion has been acknowledged to be exact, but the interpretation is still under discussion.

All the nutritive phenomena which we have thus far studied are produced under the influence of external causes; once established, they may be transmitted by heredity. But the disorder is often more marked in the offspring than in the parents; the daughter cells, younger, and, consequently, more impressionable, exaggerate the nutritive disorders which external causes had induced in the mother cells. In this manner diatheses are developed.

Diatheses.—The meaning attached to this term has considerably varied. Some authorities speak yet to-day of tubercular, syphilitic,

and cancerous diatheses. These expressions are evidently deplorable. Tuberculosis and syphilis are infectious; cancer is a disease unknown in its essence, but does not enter into the group of diathesis. In order to leave to the word diathesis a precise meaning, we must, following Dr. Bouchard, define it as a *morbid temperament*; and this is, by the way, its traditional meaning. Hippocrates called diathesis the manner of being, and admitted a diathesis of health and a diathesis of sickness—that is, as we say to-day, a normal temperament and a morbid temperament.

What, then, is temperament? It is the dynamic state of an individual as opposed to the constitution, which is applied to his static state or structure. Temperament is the expression of physiological activity—viz., nutritive activity. We are thus led to define diathesis as a *particular mode of nutrition*.

Accordingly, the number of diatheses is considerably reduced. With Dr. Bouchard we admit two—scrofulosis and arthritism.

Scrofulosis corresponds to what was formerly called lymphatic temperament; for among the lesions once considered as scrofulous, several must in reality be referred to tuberculosis or hereditary syphilis, of which, until recent times, all the clinical varieties were not known.

The scrofulous child has a special appearance, quite easily recognised. The characteristics are a fine white skin, flabby flesh, long, silky eyelashes, and a large and broad nose, punctuated by spots of acne. The tonsils are hypertrophied; the eyelids are often the seat of ciliary blepharitis, subacute or chronic. These children are subject to torpid and tedious inflammations; on the skin impetigo is frequent; on the mucous membranes it is a tenacious coryza, rebellious bronchitis, and, in little girls, leucorrhœa. On the slightest lesion the lymphatic glands enlarge and remain voluminous. Sooner or later these children become tuberculous. In some cases the glands are affected; in others, the bones, the joints; and yet in others, the lungs themselves, where the disease assumes certain peculiar features, described as scrofulous phthisis.

An inquiry into the antecedents of these children shows that their parents were in ill health, generally tuberculous, often syphilitic, sometimes simply weakened or too old. At all events, it is not a microbe, but a nutritive disturbance, resulting from various causes, that has been transmitted and exaggerated by heredity. Heredity does not, however, sufficiently explain all; in many cases, other factors have added their pernicious influence: I refer to all bad sanitary conditions, life in confined air without sun, confinement to boarding schools, and particularly orphanages. From these etiological conditions we may draw a good many therapeutical indications. To remedy the scrofulous

temperament, the children must live freely in the sun, submit themselves freely to the influence of the open air, and particularly sea air; moreover, their nutrition should be stimulated by cutaneous excitations, by the use of certain medicines, like cod-liver oil and iodine, or by hypodermic injections of artificial serum.

By the side of this first diathetic type is to be placed *arthritism,* including herpetism. Quite different in its causes and manifestations, arthritism is peculiar to the higher classes, and is observed mainly in countries of advanced civilization. It develops progressively under the new conditions imposed by civilization, and is intensified from generation to generation. Little by little, the cerebral faculties become predominant, engaging all the activity of the individual; nutrition in the other parts declines; hence arthritism has been considered a sluggishness of nutrition (Bouchard) or, after Dr. Landouzy's expression, a bradytrophy.

Quite different from the scrofulous, an arthritic person is of a nervous temperament; his flesh is firm, his stoutness is greatly variable; he may be lean, dry, or, on the contrary, fat; he is precociously bald; his character is sad, but his intelligence generally bright, and sometimes remarkably so. In youth he is subject to migraine, the first visitation of which he will never forget. When a young man, he becomes asthmatic; later, he has attacks of sibilant bronchitis. About the age of twenty-five digestive disorders set in; dyspepsia and constipation often determine hepatic hypertrophy; the fatty acids, produced by defective nutrition, are eliminated by the lungs and the skin, communicating to the breath and sweat an odour of offensive character, and predisposing to various skin diseases, notably to eczema. The disorders of cellular nutrition bring in their train humoral modifications. Sugar introduced into, or produced within, the organism is not consumed; it remains in excess in the blood, and passes into the urine, thus giving rise to a special variety of diabetes mellitus—the diabetes of the arthritic, a fatty diabetes, which is liable to last years without causing notable symptoms.

Nitrogenous substances are assimilated as poorly as, perhaps even more poorly than, carbohydrates; whence result other humoral disorders, recognised by the presence in the urine of an excess of phosphates, uric and oxalic acids. These various products may even form deposits in certain parts of the organism, creating urinary or biliary calculi, or developing gout.

Of course, all these accidents are only exceptionally the lot of the same subject; they may alternate, and be replaced in an individual or in his family. A gouty father gives birth to a son subject to migraine; another is diabetic; a third asthmatic; yet another develops renal

lithiasis. We have here a series of disorders which, despite their disparity from a clinical standpoint, are, nevertheless, linked together by the fact that all originate from a nutritive disturbance characterizing the diathesis.

In the last place, in distinction from the scrofulous, the arthritic is little disposed to tuberculosis. Should the bacillus, perchance, be implanted in his organism, the disease assumes a slow, torpid course; sclerosis tends to circumscribe the process, thus developing a fibrous phthisis, often curable.

CHAPTER XII

DISTURBANCES OF NUTRITION (Continued)

Auto-intoxications under normal conditions—Organs eliminating or transforming toxic substances—Poisons normally contained in the tissues, blood, and urine—Importance of urinary toxicity—Pathological auto-intoxications—Rôle of alterations of the digestive canal, liver, lungs, skin, kidneys, and the nervous system—Auto-intoxications chemically defined.

THE study which we have just made of cellular nutrition must be completed by the act which, in the higher beings, terminates the series of nutritive mutations—namely, the rejection of the products of disassimilation. When this elimination is hindered, the substances abandoned by the cells accumulate in the system and engender disturbances which are often serious and sometimes fatal. The nutritive disturbance thus ends in processes of primordial interest in pathology: these are the auto-intoxications.

AUTO-INTOXICATIONS UNDER NORMAL CONDITIONS

The toxic substances which, as we have seen, are produced within the normal organism as the result of disassimilation and of gastrointestinal fermentation may be eliminated through numerous emunctories.

The *bile* and the *gastrointestinal secretions* remove certain useless principles; but a part of the products thus rejected are taken up by absorption and re-enter the economy. The true emunctories are represented by the skin, the lungs, and especially the kidneys.

Through the *skin* are eliminated the volatile fatty acids and various autogenous toxic substances; through the lungs escape especially water, carbonic acid, and, in a general way, all the volatile substances introduced or formed in the economy.

Most of the solid materials are eliminated through the *kidneys*, but in order that their elimination may take place, they must become dialyzable; the nitrogenous products notably must be transformed into urea. Now, the cells reject lower oxidized bodies and ammonia, at the

same time that they abandon a certain quantity of urea. The liver causes these different substances to undergo the final transformation which permits them to dialyze; the liver, then, is the collaborator of the kidneys. The result is that its disturbances profoundly modify the secretion of the urine; the urea, the true physiological diuretic, is replaced by bodies which are eliminated with difficulty, and by their passage may even produce lesions in the kidneys.

In order that the various nutritive phenomena may be regularly produced, the intervention of the nervous system, of which we have already spoken, is necessary, as is also that of certain organs which have the property of regulating cellular nutrition, either by submitting the matter to a special elaboration or by supplying the organism with an internal secretion. Besides the liver, whose function we have described, we must mention the pancreas, the thyroid gland, the suprarenal capsules, the testicles, and the ovaries.

The extirpation of the *pancreas* is followed, as Minkowski has shown, by the development of a permanent glycosuria and the habitual symptoms of lean diabetes (*diabète maigre*). Experimentation realizes what clinical experience has established. It has been known since the investigations of Lancereaux that diabetes characterized by emaciation is connected with atrophy of the pancreas, and with a sclerosis which is often of tubercular origin (Carnot). The pancreas acts, not as a digestive gland, but as an organ endowed with an internal secretion; it thus regulates the secretion, either by governing hepatic glycogenesis, or, as is stated by Lepine, by destroying the sugar through the agency of a glycocolytic ferment. It is probable, however, that glycosuria of pancreatic origin is due to some secondary disorders of the hepatic functions. Physiology has clearly shown the relations existing between the pancreas and the liver in the regulation of the glycogenic function. Therapeutics has established that certain diabetics are cured by the administration of hepatic pulp.

If we now consider another gland, which is also endowed with an internal secretion—viz., the thyroid—we see that its total extirpation is followed by manifestations no less curious: sometimes tetany develops, in other cases a very peculiar nutritive disturbance, myxœdema. The difference in the symptoms is perhaps explained by the anatomical complexity of the thyroid apparatus, which comprises two orders of glands: the thyroids and the parathyroids, which are separated or united according to the particular animal species. It seems that the lesions of the thyroids are generally followed by disturbances of slow course, characterized by mucoid infiltration of the tissues, while the suppression of the parathyroids seems to be connected with acute manifestations. Myxœdema sometimes leaves the intellect intact and

at other times induces cerebral apathy or a cretinoid state. This is due, according to Brissaud, to the fact that, in the former case, the thyroids alone are affected; while in the latter case the whole apparatus is affected. Be that as it may, the thyroid gland acts by modifying cellular nutrition, and the disorders occasioned by its extirpation are remedied when the patient ingests thyroid glands taken from an animal. One must be very circumspect, however, in this medication; the ingestion of the thyroid body has produced various accidents, and in certain cases has caused death. Only small doses must be given daily, from 3 to 4 grammes at the most, which must be stopped as soon as the first disorders appear, such as trembling or albuminuria.

That the thyroid gland acts on nutrition is well proved by the fact that its ingestion gives excellent results in the treatment of obesity, at least in certain cases; for the medication does not always succeed, which tends to prove that the mechanism of this morbid state is very complex.

Analogous facts have been observed with regard to the suprarenal capsule. Lesions of this organ give rise to a particular syndrom—Addison's disease—characterized by two principal symptoms: melanodermia, which is rather dependent upon concomitant lesions of the solar plexus, and asthenia—general weakness—decidedly due to alteration of the capsules. In fact, it has been shown by certain physiological researches that the function of these organs is to neutralize the toxines which arise during contraction of the muscles. Attempts have been made to treat patients suffering from Addison's disease in the same manner as in myxœdema—that is, by the use of suprarenal capsules; the method is rational, but it has not as yet led to very clear results.

It is a familiar fact that the extirpation of the *testicles* or *ovaries*, especially when practised on young subjects, is followed by very marked nutritive disorders. In the case of a boy, infantile or rather feminine forms are preserved; the pilous system remains rudimentary; the larynx does not develop; stoutness is very marked. Finally, veterinarians teach us that in castrated horses the brain is smaller than in noncastrated horses of the same stature.

In the case of women, double ovariotomy results in the development of the pilous system, and especially of rapid obesity. Most of these disorders are successfully treated by the use of ovarian extracts.

Thus, the notions recently acquired in reference to the internal secretions of various organs and their rôle in nutrition have led to a new system of therapeutics—opotherapy—of which Brown-Séquard was the pioneer.

Toxic Substances of Normal Tissues of the Blood and Urine.— The second stage of nutrition, disassimilation, results in the introduction into the blood of a certain quantity of useless and harmful waste products. Thus it has been possible to say that, even normally, the organism is a receptacle and a laboratory of poisons (Bouchard). All parts of the body contain some posions. These are, first, the tissues, the extracts of which prove rapidly fatal when injected into the veins. In making cold macerations of the liver or muscles in salt water, it is found that in order to kill 1 kilogramme of animal the extract of 14 to 20 grammes of liver or 90 to 95 grammes of muscle must be injected into the veins. The greatest part of the toxicity depends upon albuminoid matter; and hence the extracts prepared hot are far less toxic. In order to kill 1 kilogramme, the extract of 117 grammes of liver or of 216 grammes of muscle must be introduced.

The substances thus entering into the constitution of the tissues pass into the blood more or less modified, but they only traverse this liquid. Hence the blood has very little, if any, toxicity, at least when it is transfused between animals of the same species; for the blood or the serum of one species is toxic for animals of different species. In operating on rabbits, it has been possible to determine in the following way the toxicity of the serum—viz., the amount necessary for killing 1 kilogramme of animal by intravenous injection: *

Horse serum .... 80 cubic centimetres.
Chicken serum....................... 20 "
Calf serum.......................... 13 "
Human serum .... 10 "
Cattle serum........................ 8 "
Eel serum .... 0.05 "

Now that therapeutics has so often recourse to serum injection these facts have a practical interest. It should be noted, however, that the results are not similar in man and in the rabbit. Horse serum, so well supported by the rabbit, produces in man numerous disturbances even in minute doses: arthropathies, fever, erythemata, albuminuria. On the contrary, the cattle serum, five to ten times more toxic for the rabbit, seems to be better borne by man. Dr. Beclère has proved its innocuousness by injecting smallpox patients with the serum of vaccinated calves in doses as high as one fortieth of the body weight.

This toxicity of the serum it is very important to know; but we

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* In all these experiments the injections were made into rabbits by the intravenous route. All the results are based on the scale of the animal kilogramme, and the figures are obtained by dividing the dose which proved fatal by the weight of the rabbit.

are not concerned with its study, for it is a question of the action of albumins of the foreign blood, albumins which evidently are not toxic for the animal from which they are derived. As to the true poisons, they should be looked for, not in the blood, where they do not sojourn, but in the fluids through which they are eliminated. From this point of view, it is the urine that has been most often studied.

Urinary Toxicity.—The brilliant researches of Feltz and Ritter, and especially those of Dr. Bouchard, have finally established that the urine contains numerous toxic substances to which three sources may be assigned: alimentation, gastrointestinal fermentation, and disassimilation.

In order to determine the toxicity of a urine, the whole amount passed in twenty-four hours is collected. The liquid having been filtered, it is then injected into a rabbit through a peripheral vein and at a uniform rate. When the animal is dead the amount of urine introduced is noted and the figure obtained is divided by the weight of the animal; thus is determined the dose fatal for 1 kilogramme. This is what is designated as a *urotoxia.*

On an average, a man eliminates in twenty-four hours 1,200 cubic centimetres of urine, the toxicity of which is 40 cubic centimetres per kilogramme; the total urine kills $\frac{1200}{40}$—that is, 30 kilogrammes; therefore it represents 30 urotoxias.

If the man weighs 65 kilogrammes, a very simple calculation shows that in fifty-two hours he eliminates an amount of poison sufficient to kill his own weight. In twenty-four hours 1 kilogramme of this man eliminates an amount of poison which would poison 0.460 kilogramme. This is the *urotoxic coefficient,* which is obtained by dividing the number of urotoxias passed in twenty-four hours by the weight of the individual; the average of numerous experiments made from this point of view has given the figure 0.461 kilogramme.

The substances which give the urine its toxicity are not well known from a chemical point of view. It is only known that there exist a mineral toxic matter (potash), toxic colouring substances, and poisons similar to ptomaines; it is also known that separation can be secured by means of solvents, such as alcohol, ether, or chloroform, or else through dialysis. It has thus been possible to determine that the urine contains at least ten toxic substances, which are well characterized by their action on animals:

1. A diuretic substance, of little toxicity, even of some value, since it assures diuresis—viz., urea.

2. A narcotic substance, soluble in alcohol.

3. A sialagogue substance, equally soluble in alcohol.

4. A convulsive mineral substance, potash.

5. A convulsive organic substance, which is precipitated by alcohol.

6. A miotic substance, insoluble in alcohol.

7. A hypothermizing substance, which is not dialyzable.

8. A thermogenic substance, which is dialyzable.

9. A mineral poison, potash, arresting the heart.

10. An organic poison arresting the heart.

The toxicity of the urine resulting from these diverse poisons varies considerably even under physiological conditions. It is possible, in the first place, to restrain it by modifying alimentation, chiefly by diminishing the potash salts; by a milk diet, and, according to Marette, especially a diet composed of milk and rice notably diminishes the urinary toxicity. On the other hand, we may obtain a similar result by favouring oxidation, either by submitting the subjects to the action of compressed air or by causing them to take moderate exercise. If, however, muscular work is pushed to the point of fatigue, cellular waste increases in great proportion and renders the urine very toxic. The examinations which have been made after long rides on the bicycle leave no doubt in this respect. In the experiments of Drs. Tissié and Sabrazes, the urotoxic coefficient in individuals who took part in the run from Paris to Bordeaux reached 2.35, which was five times greater than the normal.

Without dwelling on the toxicity of other organic secretions, we shall only remark that the bile is toxic in doses of 4 to 6 cubic centimetres per kilogramme; that the gastric juice, the pancreatic juice, and the sweat also give rise to disturbances when they are injected into the veins. Finally, according to Brown-Séquard and d'Arsonval, the expired air contains a poison similar to volatile ptomaines. Although it has been contradicted, this last result is interesting; it explains the noxious effects of confined air.

Now that we are acquainted with the toxic substances which are produced under normal conditions, it will be easy to understand what occurs in pathological states.

PATHOLOGICAL AUTO-INTOXICATIONS

The digestive canal represents the principal apparatus for the production of auto-intoxication. The fermentations occurring therein are exaggerated under a great number of circumstances; in others, the toxines produced are not completely eliminated. Whether it be an attack of indigestion, dyspepsia, or a case of dilatation of the stomach, whether diarrhœa, constipation, or even intestinal obstruction be produced, the results are the same. An auto-intoxication is induced, attended with numerous disturbances to which we have already referred when speaking of digestive fermentations. There are headache,

weakness, a general exhaustion, sometimes more serious disorders, such as aphasia; and, lastly, two phenomena which have recently been well studied, tetany and diaceturia.

Tetany, to which we have already referred in speaking of the thyroid gland, is generally observed in cases of hyperchlorhydria. Hydrochloric acid, when produced in excess, gives rise in nitrogenous matter to the development of toxic substances which Bouveret, Devic, and Gassaet have isolated. The disturbances have nothing special from a symptomatic point of view, but they are very often grave and have sometimes caused death.

Diaceturia is also a phenomenon of a toxic order, giving rise to a very serious syndrome—namely, dyspeptic coma. We shall again refer to it when speaking of auto-intoxications of diabetic origin, where diaceturia is of more frequent occurrence.

Auto-intoxications of Hepatic Origin.—The production of poisons being normal or exaggerated, disturbances may occur as the result of some derangement of the organs which neutralize or eliminate toxic substances.

To the first group belongs the liver, which arrests, transforms, and neutralizes the substances brought to it by the portal vein. When the hepatic cells are altered, this protective rôle is diminished and sometimes even abolished.

We can recognise the power of the liver by several procedures. Numerous experiments have demonstrated that the various functions of the hepatic cell are united, interdependent: when one is disturbed the others are affected. At the same time that the liver ceases to arrest the poisons it no longer elaborates the biliary pigments in a normal manner and urobiline is found in the urine. It no longer acts on the nitrogenous matter, and the amount of urea is diminished, or at least the proportion between the nitrogen of urea and the total nitrogen; albuminuria and peptonuria may be produced. But, chief of all, the liver ceases to retain the carbohydrates, and sugar passes into the urine when the portal vein contains an excess of it—that is, after meals—and alimentary glycosuria follows. The patient is given in the morning, before breakfast, 150 to 200 grammes of sirup; then the urine voided during the following four or five hours is collected; if the liver is normal, no glucose is found; if the glycogenic function is disturbed, glucose will pass into the urine. But several conditions may interfere with the results. Although the liver may be insufficient, glycosuria may not make its appearance, either because the intestinal absorption is hindered or because the capacity of the cells for consuming sugar is increased, or, finally, because the renal emunctories are not performing their work normally.

We may also determine the state of the liver by studying the elimination of various substances which this gland retains, at least partially, under normal conditions. Thus it is possible to investigate the manner in which the urine excretes the quinine salts, and especially how the lungs eliminate sulphuretted hydrogen. The latter method has been employed thus far on animals only, but it has already afforded valuable information. It suffices to inject a certain amount of a solution of sulphuretted hydrogen into the rectum; the liver arrests this gas; but, if this organ is altered, more or less considerable quantities pass into the expired air, where it is easily detected by means of lead-acetate paper placed before the nostrils.

A procedure that gives good results, but which, unfortunately, is not practical, is the study of urinary toxicity. Researches pursued in this direction have demonstrated that, if the antitoxic power of the liver is preserved, the urine, even when charged with biliary pigment, is not more toxic than normally. When the cells are profoundly affected, the urine contains from four to five times more poisons; at least that is what occurs when the kidneys are permeable. If these glands are altered, the poisons are retained in the organism and quickly bring about a fatal termination.

The fact that the urinary toxicity always increases whenever alimentary glycosuria exists further demonstrates the correlation existing between the different functions of the liver, notably between the glycogenic and the antitoxic action.

These physiological data in the rôle of the liver in intoxications find numerous applications; they explain one of the most interesting syndromes of pathology—namely, icterus gravis.

Under this name is described a complex morbid state, including three varieties, according as it may be a question of an infectious, a toxic, or a dystrophic process.

Infectious icterus gravis may be due to the most common microbes—streptococcus, and particularly the colon bacillus. It is observed in young subjects, sometimes in epidemic form, and in soldiers after overexertion. It may also occur in individuals exposed to mephitic vapours, or who have inhaled sewer gas, or have worked in the soil. In women, pregnancy and the puerperium represent indisputable predisposing causes. The disease is essentially characterized by the occurrence of an always serious icterus with fever, accompanied by disorders of the nervous system and hemorrhages, which indicate the profound intoxication of the organism. The first clinical form of icterus gravis is often cured, generally after a urinary crisis—i. e., a sudden increase of the renal secretion, which throws out the poisons accumulated during the course of the disease.

A second variety of icterus gravis is that which is induced by poisons capable of provoking degeneration of the hepatic cells, of which phosphorus is an example.

Lastly, the third group comprises the secondary forms of icterus gravis, which terminate the evolution of the various affections of the liver—cirrhosis, hydatid cyst, cancer, and passive congestion of the liver. Disturbances which rapidly grow worse are developed, such as hemorrhages and nervous manifestations, and the individual finally succumbs to hepatic insufficiency.

These three varieties, while quite distinct from an etiological standpoint, are similar in their clinical manifestations. In fact, they are all due to the same process. All the causes which we have mentioned induce degeneration of the hepatic cells. Although the point of departure is different, the results are alike; the process is always dependent upon suppression of the functions of the liver.

It is therefore at present easy to explain the mechanism of icterus gravis. The ancient theory which assumed the passage of the bile into the blood is no longer tenable, for no one would be able to understand why mild icterus should exist. The idea of Frerichs, who supposed an accumulation within the organism, not of the bile, but of products which were to be elaborated in the liver for its formation, is not supported by conclusive proof. Impressed with the inadequacy of the hepatic theories, Whitla and Decaudin have attributed the principal rôle to concomitant alterations of the kidneys. There is some truth in this view. It is certain that in persons suffering with Bright's disease, all cases of icterus are of a very serious prognosis. Nevertheless, there are cases in which the kidneys are permeable, and yet accidents occur. The principal rôle, therefore, is to be attributed to hepatic disorders. But it is not in the bile-producing function of the liver that an explanation of the disturbances is to be found, it is rather in the study of its antitoxic function. When the cells have become insufficient, the numerous toxic substances which should be retained and annihilated by the liver pass freely through the gland and impregnate the system. Icterus gravis may therefore be defined as an auto-intoxication dependent upon insufficiency of the liver. It is conceivable that the most varied causes may give rise to this syndrome; all that is necessary is the production of a diffuse degeneration of the hepatic cells.

Auto-intoxications of Pulmonary, Cutaneous, and Renal Origin.— In addition to the liver, various glands are charged with the duty of preventing the intoxication of the organism. We have already indicated the rôle of the thyroid gland and of the suprarenal capsules. We shall now consider the organs concerned in the elimination of poisons.

The lungs and the skin belong to this group. The action of the lungs, however, is much more important than was once believed. At the present day it is known that the lungs not only eliminate volatile substances, but neutralize alkaloids, such as nicotine, the sulphates of strychnine and atropine, organic acids, and salts, such as arsenite of potash. Their action is not exercised unless respiration be normal. The process is probably one of oxidation.

The skin seems to eliminate volatile substances only. When the exhalation of the skin is suppressed, as is the case when the body of an animal is varnished, death supervenes in coma accompanied by a fall of temperature, scanty urine, albuminuria, and sometimes hematuria. The effects are the same when an extensive, even though superficial, burn abolishes the action of the skin, or when the integument is the seat of extensive dermatoses.

The kidneys also come to the assistance of the organism. To a certain extent they can make up for the cutaneous as well as for the hepatic insufficiency, and eliminate the excess of poisons. But, finally, in consequence of the excessive work imposed on them, or as the result of the continual passage through them of anomalous substances, they in turn become altered and incapable of depurating the organism. Then a new syndrome develops—namely, uræmia.

Uræmia is to the kidney what icterus gravis is to the liver. It is a syndrome resulting from an auto-intoxication dependent upon renal insufficiency, which, of course, means that this morbid state may appear under the most dissimilar conditions, such as occur during the course of infections, intoxications, whether of exogenous or endogenous origin, and all processes capable of altering the epithelia of the kidneys.

The mechanism of uræmia has long been a subject of discussion. It was once attributed to the systemic accumulation of urea; but this substance, on the contrary, far from being toxic, serves to assure diuresis, and its subcutaneous introduction gives good results in the treatment of certain cases of renal insufficiency. Urea being easily transformed into ammonium carbonate, this salt was next looked upon as the causative factor. This theory contans a great deal of truth, but it appears to be too exclusive. In reality, uræmia is a complex intoxication, due to the retention of various poisons the presence of which in the urine has been demonstrated by experimental analysis. But we can understand that according to the nature, extent, and profundity of the renal alterations certain substances may be able to traverse the filter and that others may be retained. Probably this explains the diversity of the disturbances and the variability of the clinical manifestations, which have been grouped under three principal heads,

according as nervous, gastrointestinal, or dyspnoic phenomena predominate.

It would not, however, be proper to simplify the theory too much, or to imagine that uræmia is due to retention of urine, or that intravenous injection of this liquid produces in animals disturbances identical with those observed in man. In reality, the facts are more complex. The urinary poisons stored up gradually act upon the nutrition of the cells. Accumulating in the blood and the tissue fluids, they completely modify nutritive exchange. What proves this is that the blood serum contains albuminoid substances which differ in their toxic properties from those which are normally found there. In fact, it has been recognised that the blood of uræmic subjects is very toxic for the rabbit. This result does not at all demonstrate the accumulation of substances which should be eliminated by the urine, for the toxicity of the serum depends upon albuminoid substances— namely, substances which are not at all concerned in urinary toxicity. This, however, is not a sufficient reason to deny the accumulation of urinary poisons within the organism, for this secretion is very slightly toxic in cases of renal insufficiency; we mean that only these poisons, once retained, induce profound modifications in the elaboration of albuminoid matter.

Insufficiency of the liver and, secondarily, of the kidneys also explains the development of *puerperal eclampsia*. The presence of albumin in the urine of a pregnant woman often enables us to foretell the imminence of this formidable manifestation. The study of the serum establishes that this liquid is very toxic and can kill in minute doses of from 3 to 6 cubic centimetres. This toxicological research is not merely of speculative interest. Experience demonstrates that the prognosis remains good, despite the gravity of the symptoms, when the serum is feebly toxic. On the other hand, a very toxic serum must lead to a grave prognosis, even though the symptoms be mild.

Auto-intoxications in Nervous Affections and Infections.—Extremely interesting researches have also been pursued in connection with auto-intoxication in mental affections. As a rule, the toxicity of the urine is increased, and sometimes it presents particular characteristics connected with the state of the patients. According to Brugia, the urine of excited persons is convulsive, while that of depressed individuals produces prostration and considerable hypothermia. Finally, turning his attention to a paroxysmal disease—viz., epilepsy— Dr. Féré established that the urine, which is very toxic and strongly convulsivant before an attack, afterward becomes feebly toxic and slightly convulsivant.

The study of infectious diseases has particularly given rise to numerous researches. We have already said that intoxication plays the principal part in all infections. Toxic substances are referable to three sources: Some are produced by the pathogenic agent; others are derived from gastrointestinal fermentations, generally increased; and still others are due to exaggerated or perverted cellular disassimilation. If we remember that in every infectious disease there is an alteration of the glands charged with the destruction or elimination of poisons—that the liver, the kidneys, the thyroid gland, the suprarenal capsules, and the skin are more or less affected—we must conclude that all work together to prevent the depuration of the organism.

The disorders in the elaboration of the materials of nutrition affect the composition of the urine, which is found to contain extractive matters and amido acids in excess, and often anomalous substances, such as serine, globulines, and albumoses. It is probable that the toxicity so marked in the blood and urine is due to modification of albuminoids. Even injected into beings of similar species, the urine derived from infected animals causes death in minute doses of from 10 to 15 cubic centimetres. By injecting into rabbits the serum of individuals suffering from pneumonia, Rummo and Bordoni found that instead of 10 cubic centimetres, which is a fatal dose under normal conditions, the toxicity is from 5 to 6 cubic centimetres, and before defervescence may reach 0.8 cubic centimetre. In studying the serum of typhoid patients, the same authors observed that the fatal dose, which varies within normal limits during the first week of the disease, rises during the second week to a point represented by 2 cubic centimetres and even 1 cubic centimetre; then it diminishes, and is again reduced to its usual figure during the following week.

The variations in the toxicity of the urine are not necessarily parallel with those of the toxicity of the serum. As a rule, they follow reverse directions. An especially striking example is seen in pneumonia; while the serum becomes more and more toxic as the disease advances, the toxicity of the urine diminishes. On the eve of the crisis it falls to its minimum, then it abruptly rises. Therefore we may suppose that during the course of the disease nondialyzable substances accumulate in the economy and impart to the blood its toxicity. At the moment of convalescence these probably undergo a transformation, rendering them dialyzable; there must be produced a dislocation of very unstable albuminoids, which fact explains why there are found in the urine ptomaines, which certainly are derived from the primary poison, the presence of which in the blood is demonstrated by experiment.

Auto-intoxication chemically defined.—Parallel with the auto-intox-
ications which we have thus far studied, and in which the complex
phenomena are due to various chemically ill-defined poisons, must be
placed those intoxications due to well-determined substances.

We shall note lacticæmia—i. e., the accumulation of lactic acid in
the blood. It occurs when oxidation is hindered—e. g., in asphyxia,
infectious diseases, and poisonings by phosphorus and carbonic oxide;
it may also be observed in gastrointestinal affections and in diabetes,
where lactic acid is found associated with diverse organic acids. This
excess of acids in the blood explains the pains in the bones of dia-
betics, and it also accounts for rickets induced by gastrointestinal
disorders.

In speaking of digestive auto-intoxication we noted a special syn-
drome—i. e., the dyspeptic coma related to diaceturia. This syndrome
is chiefly observed in diabetics, and particularly in those who, on the
advice of their physician, eat too much meat. We then observe the
various phenomena characterizing this morbid state, occurring in most
cases in consequence of fatigue or a journey. At all events, the symp-
toms are very simple and three in number: a sharp pain in the epigas-
trium; a progressive obnubilation, terminating in coma; a respiratory
type, designated Kussmaul's coma, characterized by breathing divided
into four periods—a brisk inspiration, a pause, a brisk expiration, and
a pause. Along with these disorders, or prior to their appearance, a
characteristic phenomenon is produced—that is, a special odour ex-
haled by the breath and urine of the patient—a strong odour recalling
that of chloroform. It is attributed to acetone, whence the name ace-
tonæmia or acetonuria, often given to the syndrome. But if acetone is
in fact produced under these circumstances, the disturbances are rather
attributable to a similar body, ethyldiacetic or acetylacetic acid. It is
this acid that is brought to light by the following test, which should
always be resorted to in these cases: The urine being placed in a test
tube, a few drops of perchloride of iron are poured along the side of
the tube. The iron, by virtue of its density, falls to the bottom of the
test tube, and if ethyldiacetic acid exists, the perchloride assumes a
brownish-red colour, resembling that of Bordeaux wine. The reaction
is not absolutely characteristic, for it is also produced when the pa-
tient has ingested antipyrine. This source of error, however, is easily
eliminated.

Apart from ethyldiacetic acid, the urine contains other acids, such
as lactic and β-oxybutyric acids. This led to the belief that it would
be possible to prevent accidents by neutralizing these acids, by intra-
venous injections of solutions of sodium bicarbonate. The attempt
was rational, but it has as yet given no results.

Aside from diabetes, diaceturia may be produced in the following conditions: In persons subsisting on a meat diet; in certain forms of dyspepsia, where it engenders coma similar to diabetic coma, but differing from the latter by the absence of Kussmaul's respiration; in the course of certain infections, and in asphyxia.

Among other chemically defined auto-intoxications must be mentioned that caused by *uric acid*, which is derived from nuclein—that is, from cellular nuclei. The excessive production of this agent gives rise to the development of gout. We must also mention *ammoniacal intoxication*, which occurs in infectious diseases, and especially in affections of the digestive canal and of the liver; intoxication by anomalous *albumins* and the *albumoses*, which are produced under a great number of circumstances already referred to; intoxication by *ptomaines*, the genesis of which we have pointed out; and, finally, intoxication by *volatile substances* originating in the alimentary canal —sulphuretted hydrogen and methylmercaptan.

If we consider the numerous data furnished by the study of autogenous poisons, we see that the living organism is always in danger of intoxication, even under normal conditions. In diseased states poisons increase because new substances are produced by pathogenic agents, gastrointestinal putrefaction is exaggerated, and cellular disassimilation is more active and often deviates from the normal type. These chemically ill-defined poisons have been well studied experimentally. Moreover, it has been established that the organism possesses several means of protection against them; it transforms and eliminates them and produces antitoxic substances which counterbalance and neutralize their effects. When one of the protective organs is attacked, others replace it; for instance, the liver and kidneys can replace each other to a certain extent.

This study of auto-intoxications has demonstrated that numerous morbid phenomena originate within the organism. There is no exception here, however, to the rules already laid down. In fact, the disturbances are secondary, and always referable to an external cause. There are thus produced, directly or indirectly through the nervous system, cellular disorders, which secondarily give rise to humoral modifications. These derangements and modifications may be transitory, or they may become permanent; in a great number of cases they may be transmitted to descendants. We are thus led to the study of the pathology of the fœtus and of heredity.

CHAPTER XIII

PATHOLOGY OF THE FŒTUS—HEREDITY

Pathology of the fœtus—Passage of toxic substances and of microbes through the placenta—Congenital infections—Malformations—Transmission of certain acquired characters—Heredity—Influence of each generator—Consanguineous marriages—Maternal impregnation—Atavism—Heredity of nutritive disorders: diathesis—Heredity in toxic and infectious diseases—Nervous heredity—Superior and inferior degenerates—Genius, insanity, crime—Conclusions.

ALTHOUGH protected in the uterine cavity, the fœtus is not entirely beyond the reach of external agents. It may suffer traumatism; it may be exposed to the influence of the surrounding modifications of a physical order; it may be assailed by toxic substances or animate agents entering through the only channel which connects it with the external world—through the placenta and the umbilical vein. Diseases or lesions may thus be produced which must be considered as *congenital* and not hereditary.

Intoxications.—The passage of toxic substances from the mother to the fœtus has been repeatedly studied. Since the old experiments of Mayer (1817) and Albers (1859) and those of Dr. Porak, a great many facts have been discovered throwing new light upon the question. We now know that lead, arsenic, the iodide and bromide of potassium, and phosphorus may pass through the placenta. The last-named substance at times produces placental hemorrhages and causes a characteristic fatty degeneration in the liver of the fœtus. Iron and mercury do not pass from the mother to the fœtus, although mercury accumulates in the placenta. Most of the colouring substances do not impregnate the fœtus; yet Flourens observed that the bones and teeth were red in a pig whose mother had ingested madder during gestation. The intraplacental transmission of alkaloids, opium, atropine, quinine, etc., is generally conceded to-day.

Certain clinical and experimental facts also prove that carbonic oxide may reach the fœtus; but the quantity contained in its blood is six times less than that found in the mother. This proportion, more-

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over, expresses a general law: Weights being equal, the fœtus contains a less amount of toxic substances than the mother, and its tissues offer a much greater resistance to intoxication. Living fœtuses have been extracted from the uteri of women and animals killed by chloroform, chloral, or asphyxiation. A very interesting experiment by Savory positively established this fact: If one of the fœtuses be extracted by laparotomy from the uterus of a pregnant female and be returned to the womb after having received a strong injection of strychnine, fatal convulsions will be produced in the mother in consequence of the passage of the alkaloid from the fœtus to the mother through the placental circulation. The fœtus is in no way affected, and, if sufficiently developed, a Cesarean operation may save it. It withstands, then, a much stronger dose of strychnine than suffices to kill the mother. The fœtus may die in a case of poisoning, but its death is then brought about by the fall of blood pressure in the mother.

Let us now consider the organs qualified to protect the fœtus against poisons. As poisons are always brought in by the umbilical vein, they first travel through the liver. This organ acts as in the adult; it arrests and destroys the toxic substances, provided it contains glycogen. Now, the researches of Claude Bernard have shown that glycogen exists in the embryo at first only in a diffused state, and that it is only from the second half of gestation onward that it localizes itself in the liver; it is from this period that this organ exerts its protective functions.

The poisons not destroyed by the liver leave the fœtus by the umbilical artery and the placenta, and in this way return to the mother. It has been said that they are also eliminated by the kidneys. The experiments of Dr. Porak, however, do not confirm this assertion; the amniotic fluid does not contain the substances absorbed. If salicylate of sodium be given a few hours before parturition, no trace of the substance can be found in the urine of the newborn. Therefore it may be stated that renal elimination begins at birth and becomes effective only at the end of a few days.

Infections of the Fœtus.—Do microbes, like poisons, pass through the placenta? The answer is not a matter of doubt; the existence of congenital smallpox and syphilis is an incontrovertible demonstration of the passage of microbes from the mother to the product.

The memorable experiments of Pasteur on silkworms furnish very interesting results in this connection. Two diseases exist among silkworms, pebrine and *flacherie*. The germs of pebrine may pass from the mother to the eggs and to the young; the male does not transmit the disease, but produces a debilitated progeny. In *flacherie*, on the

contrary, neither the male nor the female can transmit the infection; but if one of them has contracted the disease, the offspring is weak and evinces a well-marked tendency to acquire the disease.

Analogous facts are observed in man and in mammals. The first experimental researches, in this case as in all the others, were undertaken with anthrax. Brauell and Davaine, the experimenters who began the study of the question, obtained negative results only, and affirmed that the placenta is a perfect filter. This law of Brauell-Davaine is false, as Straus and Chamberland have shown. But the number of bacilli which pass through the placenta is minimal, and microscopic observation does not suffice to reveal their presence; only cultures made with large quantities of liver will do so. In this manner positive results are obtained in about half the cases. The problem as to the cause of these inconstant results has been taken up by Dr. Malvoz. According to this author, the *Bacillus anthracis* passes through the placenta only when this organ is altered. The problem, therefore, as to what are the causes of the localization of microbes in the placenta as well as in other organs resolves itself into a much wider question, and one which we can not satisfactorily solve, although we have some data bearing upon it. However this may be, the results are identical in man. In four published observations the fœtus of a mother suffering from anthrax twice contained the bacterium (Marchand, Paltauf), twice it did not (Eppinger, Morisani).

Among the other microbes which may produce fœtal infection may be cited the pneumococcus, which may cause a much more serious disease than in the mother. In an observation of Thorner, a woman was delivered the day after the defervescence of a pneumonia; the child died thirty-six hours later. The autopsy revealed hepatization of the lower lobe of the left lung and the presence of pneumococci. Netter has reported a case of congenital infection in which pneumococci invaded the lungs, the pleura, and the meninges.

Relatively numerous observations establish that the bacillus of Eberth may pass through the placenta; but it does not produce any lesion in the fœtus, no alteration of Peyer's patches, and no splenic hypertrophy. It causes a true septicæmia.

It is different with smallpox. There are on record a certain number of observations of congenital smallpox in which the child came into the world with the pustules characteristic of the disease. In most cases it had not advanced so far in the child as in the mother. This proves that their infection had not been simultaneous. It goes without saying that contamination is not a constant occurrence; in twin birth one of the children has been known to be affected and the other not. Finally, vaccinated women living in an epidemic centre,

without being themselves affected, have given birth to children covered with pustules.

The other eruptive fevers are also observed in the fœtus, but only exceptionally.

The transmission of various infections, such as glanders, hydrophobia, cholera, and paludism, has also been observed. Although very interesting, these facts add nothing new to the history of congenital infections. On the other hand, highly important results have accrued from the study of two chronic infections—namely, syphilis and tuberculosis. While the preceding diseases have a rapid evolution and can be communicated only by the mother, in syphilis and tuberculosis the influence of both parents must be taken into account.

Hereditary Syphilis.—When the mother is syphilitic, there are several possibilities. In certain cases placental lesions exist and bring about abortion. The frequency of this occurrence is well known; and repeated abortions, if otherwise unexplained, must always suggest syphilis. In other cases the child is born with specific manifestations upon the skin and mucous membranes. A third class of facts is made up of those in which the child, normal at birth, shows syphilitic affection toward the sixth week; various eruptions appear, particularly blebs of pemphigus, which, when located upon the soles of the feet, are absolutely characteristic. But the specific lesions may appear much later—for example, after fifteen or twenty years. This is what is known as retarded hereditary syphilis.

When the father alone is syphilitic, the same possibilities exist, and abortions are particularly frequent. But, what is more remarkable, the fœtus may be syphilitic while the mother remains sound. Nevertheless, in such cases the maternal organism is altered, since it has acquired immunity from syphilis. This is known as the law of Colles, which, from a practical standpoint, may be expressed as follows: A woman who has been delivered of a syphilitic child, if she remains unaffected, can suckle her nursling without exposing herself to contamination.

Several hypotheses have been advanced to explain this immunity. It has been maintained by some that a uterine chancre existed and passed unnoticed. If this were the case the immunity would be due simply to an infection. In support of this theory the unique observation of Lewis is cited: A woman is fecundated by a syphilitic and gives birth to a contaminated child; she remains intact. Subsequently she is impregnated by a healthy man and conceives another child, also syphilitic. Here is proof that the unknown microbe of syphilis had invaded the maternal organism. It is true that this fact admits of another explanation and could just as well be looked upon

as an instance of *conceptional syphilis*. Under this name are grouped those cases in which the organism of a woman bearing a syphilitic foetus is from the first invaded by the virus and a general infection occurs without primary lesions, but which is immediately expressed by secondary manifestations. In this case it is the microbe which has passed through the placenta from the foetus to the mother. When immunity alone is transmitted, it is generally admitted that only the soluble substances, and not the figurate elements, have traversed the filter and have conferred upon the mother a marked power of resisting infection.

When the parents are not syphilitic and the mother contracts the disease during pregnancy, two results are possible: If contamination takes place before the seventh month, the chances are that the foetus will be infected; after that time it will remain sound; and this is easily understood, since the infection has not had time to spread, because it is still local.

If a child born of a syphilitic mother manifests no trace of infection at birth, it may be suckled by its mother without danger. It has acquired immunity. This is the law of Profeta, which may be placed by the side of the law of Colles.

Hereditary Tuberculosis.—The observations made upon hereditary syphilis have been turned to account in the study of tuberculosis. At the present day it is an incontestable fact that tuberculosis is very frequent in early childhood. Dr. Landouzy, who has clearly brought this fact to light, is of the opinion that half the cases of death in newborn children are caused by this infection. Although an agreement has been reached on this first point, the operating mechanism is still a subject of contention. According to some, it is the germ which is transmitted; according to others, it is only a predisposed organism—the soil. In other words, the child may be born tubercular or with a tubercular tendency.

Incontrovertible, if not numerous, instances in which tubercles containing the characteristic microbe were found in stillborn children have been cited in favour of intraplacental transmission. In some cases the lesions predominate in the liver, which is the first organ reached by the bacilli coming from the placenta.

Analogies derived from syphilis have led to the admission that the microbe may remain inactive in some corner of the organism—in the marrow of the bones, for instance—and become active several years later, on the occasion of a traumatism or any other cause.

A delayed form of hereditary tuberculosis, more or less analogous to hereditary syphilis, is often shown by the presence of osseous or articular manifestations. This idea is supported by experiments which

prove that apparently sound fœtal organs may contain bacilli, and also by the researches of Maffucci, who, after introducing various microbes into hens' eggs, saw infection occur long after hatching.

The transmissibility of the bacillus is an undeniable fact. Congenital tuberculosis exists, but it is of exceptional occurrence. More frequently the tendency is transmitted: the child comes into the world with a vicious nutrition, which manifests itself in lymphatism, scrofula, or chlorosis, as the case may be, and creates a marked predisposition to tubercular infection.

Congenital Malformations.—Not infrequently infections become the starting point of congenital malformations. For instance, in cardiac infection the right heart, which is more active, is preferably affected. The microbes locate themselves upon the pulmonary valves, causing adhesions and consequent stricture of the orifice. The blood, unable to pass freely along its normal channel, makes its way through the temporary openings and prevents their closure. According to the period at which the lesion of the pulmonary artery has taken place, there result a permanency of the opening in the interventricular septum or of the foramen of Botal, persistence of the ductus arteriosus, compensatory development of the bronchial arteries, etc.

Most cases of congenital malformations, however, arise from another mechanism; and they are connected with *disturbances of fecundation,* as has been shown by numerous researches, most of them made upon the lower animals.

When a cell is about to divide, the nucleus presents several important modifications. The chromatic filament, constituting its principal part, increases in distinctness; it assumes a stellate form, and, finally, separates into a certain number of chromatic rods called *chromosomes,* each one shaped like a V. The number of chromosomes is fixed, and always the same for every cell of the same species. Let us suppose that they are eight in number. They arrange themselves in a circle and perpendicularly to the long axis of the cell, the vertex of the V toward the centre. In this position they form the *equatorial plate.* Meanwhile a light spot called *centrosome* has appeared at the two poles of the cell. Very soon the chromosomes divide longitudinally, thus making 16 half chromosomes in the equatorial plate. During this time filaments coming from the centrosomes have reached the apex of the divided rods, and, in contracting, draw them toward the poles. Eight half chromosomes are thus united to each centrosome, producing what has been called *amphiaster.* At this moment evolution is completed; the cellular protoplasm divides, while the chromosomes return to quiescence, fuse, and again form a chromatic filament.

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Thus the two daughter cells will each have a chromatic filament made of 8 rods, just as the mother cell.

If we now turn our attention to the ovum, we find that the germinal vesicle, the part corresponding to the nucleus, migrates to the periphery of the ovum when it has reached maturity. A division of the nucleus then takes place and produces two nuclei, each containing 8 half chromosomes. One of these nuclei leaves the cell. This is the *first polar globule*. The remaining nucleus, instead of returning to quiescence, immediately divides. The chromatic filaments do not have time to grow, and, consequently, can not further subdivide. But the two nuclei come into existence in another way: The half rods arrange themselves in groups of 4 and form two semiamphiasters; we thus have two half nuclei. One of them, the *second polar globule*, located at the periphery, leaves the ovum; the other remains and constitutes the *female pronucleus*.

Thus this cell, primarily containing 8 rods, first undergoes division, producing 16 half chromosomes. Eight of these leave the cell with the first polar globule, and 4 of the remaining 8 leave with the second polar globule. Four only remain in the ovum. Consequently, the ovum represents but half a cell.

The spermatozoon also represents a half cell. It is born in a cell called male ovum, which, instead of dividing into two, splits into two twice in succession without interval of rest. Thus a male ovum produces 4 spermatozoa, each possessing half of the chromatic rods belonging to a normal cell.

When fecundation takes place, a spermatozoon penetrates the ovum. This spermatozoon consists of a head corresponding to the chromosome, an intermediary part answering to the centrosome, and a tail, a mere organ of locomotion similar to the vibrating cilia of certain cells. As the result of a special attraction, the head and the body, making up the *male pronucleus,* advance toward the female pronucleus, which has resumed its place at the centre of the ovum. When the two elements meet, the chromosomes unite, and from the fusion of the two half nuclei a complete nucleus with the required number of chromosomes results. As to the centrosomes, they divide into two; then, after performing an evolution of 90 degrees (quadrille of Fol), they come in contact. As a result of contact two new centrosomes composed of a male semicentrosome and a female semicentrosome are produced. Thus a complete nucleus is formed, called the *yolk nucleus.*

This nucleus divides regularly. Every cell of the body is derived from it. Each one of these cells acquires the same number of chromatic rods as the initial cell, and each of them also contains an exactly

equal part of the male and female elements. The process of karyo-kinetic division insures the equal distribution of the two substances in every cell.

Under normal conditions, one spermatozoon fertilizes the ovum, but under certain abnormal conditions several spermatozoa find their way into the egg. From two to ten have been observed in one ovum. Beyond this number the egg succumbs. Recent researches, particularly those of Fol, have made a successful beginning in the search for the cause of these anomalies of fecundation. Several spermatozoa may penetrate the ovum when fertilization takes place before perfect maturity of the egg. Under these conditions the enveloping membrane is not yet sufficiently resistant; it does not close in quickly enough after the passage of the male element, and through the opening thus left other fecundating cells may enter. The result is the same when fertilization occurs too late, since the enveloping membrane has then lost some of its strength. Moreover, hyperfecundation takes place when the egg comes from a weakened, sickly animal, or, as Fol has shown in his experiments on sea urchins, when it is anæsthetized by a current of carbonic acid.

If two spermatozoa penetrate the ovum in consequence of one of the causes just stated, segmentation of the germinal vesicle gives birth to four amphiasters, and, consequently, to two cells, which separate and become the centre of two embryos. It was formerly believed that this double fecundation was due to the existence of two nuclei in the same ovum; we now know that it is due to double fertilization of a single nucleus.

The two primitive lines found in cases of double fecundation develop parallel to each other; from this a twin pregnancy results. The two beings have one and the same origin; they represent one being divided into two. It follows from this genesis that they are always of the same sex, and that a striking physical and moral likeness is to be expected. They may have the same thought at the same moment; a sentence begun by one of them may be completed by the other. These cases must not be confounded with the twin births resulting from the intra-uterine fecundation of two ovules which produces two different beings of the same or of a different sex. This must be looked upon as the reappearance in man of a phenomenon which is of normal occurrence in most animals.

When two fœtuses develop in the same ovule it may happen that the two primitive lines meet and fuse at a specific instant, thus occasioning the formation of a *double monster*. The several varieties observed under these circumstances may easily be brought back to a few types.

Let us suppose that the two primitive lines are in a straight line. If they meet, the two beings unite at the vertex, the rest of the two bodies remaining independent.

If they form an obtuse or a right angle, the heads and the upper parts of the trunk fuse and produce a monstrosity. The best known of this class is called *Janiceps*—i. e., a monster with a double face. The fusion having taken place when the head was open in front, the two beings have united along their anterior portions, so that each face is formed out of an equal part of each being.

When the two primitive lines meet at an acute angle, the trunk, the neck, and the lower part of the head unite.

Finally, if the lines are parallel, the fusion involves the trunk, and if they are slightly divergent, the lower extremities alone are joined.

We have thus far supposed that the two beings developed equally, and that the monstrosity resulted from a simple accidental fusion. But it may happen that one of the embryos does not develop well; a part necessary to life—the circulatory or the nervous system—may be missing, or the subject may remain in a quite rudimentary state. Unable to live of itself, it will ingraft itself upon its fellow and become a parasite, or it may penetrate into the abdominal cavity and thus become a sort of tumour.

Aside from the facts just considered, monstrosities have been known to occur even with normal fecundation. The determination of these monstrosities has been brought into evidence by important researches initiated by Dr. Dareste. The experimenter can at will cause the birth of a monster. It suffices here, as everywhere else, to call into play external agents—mechanical, physical, chemical, or animate.

For instance, if the egg, instead of being allowed to remain in its normal surroundings, be subjected to the influence of certain motions, say rapid vibrations; or if it be kept in abnormal positions—for instance, in a vertical position; or if certain cellular groups be destroyed during their evolution, as was done by Chabry, a monster will be produced.

If one wants to use physical agents, the egg may be placed in an oven too hot or too cold; or, what is a still safer means, its surface may be unequally heated. Its growth may be modified even by light rays.

Of late chemical substances have been used. Dr. Féré has produced a great number of monstrosities by exposing hens' eggs to the influence of volatile poisons, such as ether, chloroform, vapours of mercury, or by injecting into the eggs toxic substances, living microbes, or soluble products obtained from microbic cultures.

Can these researches made upon oviparous animals be applied to mammals? This question can now be answered affirmatively. Monsters are the result of external causes acting either directly on the embryo, or, what is more frequently the case, indirectly through disturbances or lesions of the membranes of the egg. Alterations of the amnion, exaggerated or insufficient secretions of the amniotic fluid, lesions of the vascular area due to compression, or the trophic disturbances they provoke, induce irregular evolution of the fœtus. The best example is that of syphilis, which frequently produces amniotic lesions and consecutively causes numerous malformations, such as spina bifida, harelip, and clubfoot.

Every defect of structure and every monstrosity can be explained as partial arrest of development or as hypernutrition.

In the first case certain parts are atrophied, others remain rudimentary, and unions fail to take place. In the second case certain parts develop excessively, or a normally transitory disposition becomes a permanent one. If it be remembered that ontogeny is the recapitulation of phylogeny, it becomes clear that the persistence of a transitory disposition represents a variation toward an existing type, or a type having existed in another species. Anomaly, then, is the reproduction of a state normal in other beings, whether living or extinct.

Most, but not all, of these anomalies may be transmitted by heredity. The remark has even been made that the deepest and strangest transformations are generally those that hardly ever persist in the descendants. As a matter of fact, the malformations we have studied —namely, those resulting from a disturbance of the normal evolution —must be clearly distinguished from those in a way merely accidental. For instance, if the umbilical cord twists itself around one or several limbs and causes amputation by pressure, we have an accident which will not be transmitted. Similarly, when an infection has produced a pulmonary stricture resulting in persistence of the foramen of Botal or of the interventricular orifice, the cardiac malformation will not be found in the descendants. Accidental lesions, whether congenital or acquired, remain isolated; they do not affect the offspring. On the contrary, when there are defects in the evolution of the ovum and when the anatomical anomaly results from a functional deviation, the leading tendency which presides over the development of the being and assures the unity of the species seems to be profoundly altered. Several generations will be required before the normal type is reproduced.

We are thus led to ask why accidental anomalies are not transmitted, while those due to functional disturbances pass to the offspring. This study brings us to the history of heredity.

HEREDITY

Heredity, says M. Ribot, is the biological law according to which living beings tend to repeat themselves in their offspring and to transmit to them their properties.

Two great laws seem to govern and explain heredity: *the law of conservation of the ancestral type* and *the law of evolution*.

The species possesses a unity, or rather an individuality, and it preserves its fundamental characteristics through the ages in such a way that men of all times and of all countries resemble each other. The likeness, however, is not perfect; certain modifications have occurred, and it is quite certain that the civilized man of the nineteenth century is not identical with primitive man. An evolution has taken place. Its significance will be better comprehended if it be remembered that the species is ruled by the very laws that govern the individual. If we consider a being from birth up to advanced old age, we observe in it the working of the two laws just mentioned. It is clear that the adult individual is no longer the same as in his childhood, and that he will still continue to alter as he advances in years. Nevertheless, in spite of these continual changes, the individual type has been preserved, and in the midst of successive transformations the immutable foundation which maintains the personality of the individual remains.

The species is neither more nor less modifiable. It evolves as well as the individual, and also passes through the three phases of growth, climax, and decay. The species is preserved through the ages, and it maintains through heredity its resemblance to itself, just as personality preserves that of the individual.

If we consider inferior beings, heredity seems much more perfect. But this is, in reality, an optical defect of our minds, if the expression be allowed. It is harder for us to grasp that which constitutes personality than to perceive the common traits. Consequently, our attention goes to the latter, and thus, because we do not see the differences, we believe that all individuals are identical and remain so. In superior beings, and particularly in man, we are in the habit of looking for the dissimilarities. On closer scrutiny, however, it is easy to convince one's self that the resemblances are always preponderant; the common characteristics are more numerous than the points of difference. Consequently, it can be said that heredity is the rule and nonheredity the exception.

The greatest naturalists and the most celebrated philosophers have taken up the study of heredity and have endeavoured to explain it. But most of their theories belong to the past. The gemmules of Dar-

win and the plastidules of Haeckel are now well forgotten. The ideas of Weissmann alone deserve our attention, although they have been vigorously criticised by most authors.

Weissmann establishes a radical difference between the reproductive and the other cells of the body. The former are eternal; they do not die, and thus they assure the perpetuity of the species. This statement, which may at first seem fantastic, finds support in the study of unicellular beings. Amœbæ perpetuate themselves by fission. It is not exact to say that one animalcule has given birth to another. There is neither mother nor daughter, but there are two sisters. Amœbæ are collateral beings; and the amœba of the nineteenth century is the same as the one which existed at the beginning of the world. If, perchance, a few amœbæ die, or the pool in which they live dries up, their death is merely a matter of accident. Nothing in the evolution of this protozoon doomed it to death. For it natural death does not exist.

The same reasoning may be applied to the generation of the cells of higher animals. The only difference is that they produce two classes of cells: cells whose function is to maintain the life of the species, and which are consequently immortal, and cells that will constitute the body, the *soma*; and are therefore destined to die.

This theory of the continuity of the germinal plasma explains perfectly the preservation of the specific type. But Weissmann pushes his theory to its utmost limits and sets up an impassable barrier between the somatic and the generating cells. He does not admit that the former may have any influence upon the latter, and is led in consequence to the absolute denial of the transmissibility of acquired characters.

At this point we must make a distinction which to us seems to be of fundamental importance. Acquired characters may be of two kinds: They may be accidental, and therefore not transmissible; or they may be due to functional modifications, and then they are hereditary. This distinction leads us to the following new conclusion: *Heredity is the transmission of functional but not of anatomical modifications.*

Those who deny the transmissibility of acquired characters generally cite the Jewish race. For more than three thousand years circumcision has been practised among them, and yet the children continue to be born with foreskins. In the same way the young of certain dogs whose tails and ears have been clipped are born with these appendages developed just the same.

On the other hand, let us consider a functional disturbance. Nothing is so instructive in this respect as the famous experiment of Brown-Séquard. If the sciatic nerve of a guinea pig be cut, the animal becomes epileptic. If it be mated and brings forth young, these will

also become epileptic. What is it, then, that has been transmitted in this case? Is it the mutilation? Not at all. The sciatic nerve in the offspring is quite normal. It is the functional disturbance alone which has been fixed by heredity.

As the development of an organ is regulated by exercise of that organ, it is conceivable that transmitted functional modifications may be accompanied by anatomical alterations as a consequence. Suppose, for example, a man to be gifted by heredity with a superior intelligence; he will come into the world with particular aptitudes which will call forth an unusual development of his cerebral cells. In other words, it is not because the brain is highly developed that the intelligence of the individual is remarkable; but the anatomical centres which serve as the substratum of the function have attained an unusual development because he has inherited a superior cerebral power.

Our conception is also applicable to congenital malformations. Those resulting from accident—for instance, amputation by the umbilical cord—are analogous to acquired traumatic lesions. They are not transmitted. Those produced by functional disorder, and those representing an arrest or an excess of development, or a return to some ancestral form, are transmitted to a certain number of generations.

The ideas just expressed are nothing more than the application of the great law that the function precedes the organ, and explains, directs, and regulates its development. Functional changes alone are powerful enough to modify the conservative rôle of heredity.

To sum up, we admit that the germ plasm goes through the ages without manifesting any tendency to modification. It preserves the individuality of the species. The somatic cells, on the contrary, undergo the influence of evolution. They are affected by external agents, and, reacting in their turn on the germinal cells, give them a new direction. They tend to modify the primitive type. After the preceding considerations, again taking up the two great laws already offered as accounting for evolution, we can say: The law of conservation of the ancestral type finds its explanation in the persistence of the germ plasm; the law of evolution finds its explanation in the modification of the somatic cells. Accidental changes are not transmissible, because they reach the soma only. Functional disturbances are hereditary when the somatic modifications they induce react upon the germinal cells. If, in this last case, anatomical changes appear, it is because the development and the structure of the organs are governed by the functions of which they are the material substratum.

It is, we believe, in this way that heredity can be understood, and that a satisfactory basis can be found for the two laws of conservation and evolution by which it appears to be governed.

Rôle of the Two Generators.—In superior beings heredity is dependent upon two factors. Theoretically, according to the date of embryogeny, each cell of the newborn animal contains the same quantity of male and female chromatine. Accordingly, it would seem that the two generators must influence the product in an equal degree. As a matter of fact, the results are not so simple. Neither the physical nor the moral resemblance is an average. One of the parents exerts a preponderant influence. Several hypotheses have been advanced to explain this result.

Orchansky claims that the parent nearest maturity imparts its sex and its likeness to the offspring. It is easy to raise objections to this theory. It is, however, sufficient to remark that in twin pregnancy children are frequently of a different sex. This fact might readily be explained if the opinion entertained by breeders be accepted. According to this view, fecundation gives a male or a female according as it occurs at the beginning or end of the catamenia. If the twins are not of the same sex, it is because two eggs have been fertilized at two different times.

Among the disorders which, without doubt, must be attributed to the collaboration of the two parents, those due to *consanguinity* deserve attention. It is a matter of common knowledge that marriages between relatives give bad results. Such unions are often sterile or the children suffer from malformations, polydactylism, albinism, pigmentary retinitis, and especially from deaf-mutism. But this is not always the case, and in many instances children born of such marriages have been perfectly normal.

As a matter of fact, the effects of consanguineous marriages are to be explained simply as the summation of common characters. As they belong to the same family, the chances are great that the parents possess the same characteristics and the same physical or moral defects. They may be slight in each one of them, but they add themselves and increase in the descendants, as they are not corrected by different defects or qualities. We conclude, then, that marriage between relatives will give good results when the pair do not possess analogous defects. Otherwise, the least defect may be considerably exaggerated in the offspring. Consanguinity must be looked upon as cumulative converging heredity.

The same remarks apply to marriages formed between individuals of the same social class, and consequently having the same aptitudes, tastes, and tendencies. It is a *social consanguinity*, which may be compared to family consanguinity. The results are evidently analogous. Heredity fixes and exaggerates various defects, but natural selection sooner or later interferes. It counterbalances the retrogressive effects

of social selection, and ends in the sterility of these degenerate families.

The influence of the father is not alone felt by the ovum he has impregnated. Individuals born later have been known to resemble the first generator in some particulars. *Impregnation of the mother*, as the phrase has it, has taken place. All breeders know that a bitch fecundated for the first time by a dog of a different race gives birth in the two successive litters to young resembling the first father, although the second impregnation was by a dog of the same race as the mother.

Cases are also cited of women of the white race who, after having had a child by a negro, have subsequently, and as the result of intercourse with a man of their own race, given birth to children on the bodies of which a few black pigmentary spots could be seen. Lingard knew a man belonging to a family in which for several generations all the males were hypospadic. This man married and had three hypospadic children. After his death his wife remarried and had four children, all of whom were hypospadic, although her second husband was perfectly formed. These four children had in their turn eleven children, only one of whom suffered from hypospadia. The structural defect transmitted as a result of the maternal impregnation had, it appears, modified her organism less deeply, since it showed a strong tendency to disappear.

These facts have such a mysterious aspect that certain authors, unable to understand them, have found it easier to deny their reality. Those who have tried to explain them have advanced three theories: One of them supposes that an imperfect fecundation of a few ova still in the ovary takes place at the time of the first fertilization. Another admits a perfect fecundation, and, moreover, supposes that the ovum waited for conditions more favourable to its development. These two hypotheses are evidently not based upon any known fact. It seems more rational to admit an impregnation of the mother by the foetus. The latter has inherited the qualities of the father; its cells have received from the father a nutritional and functional direction manifested by a particular humoral state. As a consequence of the continuous changes taking place through the placenta, certain soluble products reach the mother and impart to her various functional aptitudes resembling those of the father. After all, this theory does no more than extend to the several forms of impregnation the results derived from the study of syphilis.

All acquired characters, fixed in this way by heredity, pass from generation to generation indefinitely, until a time arrives when a character long since modified, or even lost, reappears without ascertainable causes.

This is what is called atavism. Darwin has collected a large number of examples establishing that certain characters may skip several generations. We shall again refer to these facts, which have often been put forward in an exaggerated form to explain certain nervous variations.

HEREDITY OF NUTRITIVE DISORDERS.—Among the functions whose modifications may influence heredity, the one most general must first be mentioned: *nutrition*. We shall be brief on this subject, as it has already been considered under diathesis. We have seen what part was to be ascribed to hereditary modifications in the development of arthritis and of scrofula, and we have shown how a slight taint in the parents grows worse in the descendants. The fact is striking in arthritic persons, and it easily admits of an explanation. When arthritism develops under the influence of external causes, the latter influence adult cells, which are endowed with a well-defined mode of activity. The modification, therefore, is to affect conditions of many years' standing, whereas disturbances transmitted by heredity affect young cells not yet possessed of a nutritive direction, and therefore readily influenced by the impressions they receive. In this way we adapt to the history of heredity the conditions which are the very basis of children's education. In both cases young cells yield easily to influences which they would resist in their adult state.

In considering a family of arthritics, we find in certain of its members clinical tendencies which may coexist or alternate. Among its most habitual manifestations, arthritism includes gout, eczema, nervous affections—from neuralgias and hemicrania to hypochondria and neurasthenia—fat diabetes, gravel, biliary lithiasis, etc. These various disorders may coexist in the same individual, but more frequently they alternate either in himself or in his descendants. For instance, a gouty father may have an asthmatic child. In other cases, an arthritic's son, suffering in his youth from hemicrania, becomes asthmatic when about fifteen; around thirty or forty he is afflicted with gout, and later on dies of cerebral hemorrhage. Heredity is termed *similar* when the child suffers from exactly the same disorders as the father—when they, for instance, are both asthmatic or gouty. It is called *homologous* when the manifestations are different.

Arthritism is the inheritance of civilized people and of the upper classes. Most individuals gifted with a superior intelligence are tainted by it. Geniuses are often sad, fantastic, one-sided; their cerebral aptitudes have developed unequally; they suffer from deficiencies and disorders which at times border upon insanity. In such subjects heredity may continue to emphasize the superior qualities. Much too

often it assures the predominance of the cerebral disorders and ends in mental degeneration or insanity. We shall return to these questions when treating of nervous heredity.

The second diathesis, scrofula, is found, we have said, in children born of parents in bad health, suffering from some chronic intoxication or infection: alcoholism, syphilis, and especially tuberculosis. They are weaklings with flaccid muscles, long and silky eyelashes, hypertrophied tonsils, and wide nose. During their first years they suffer from impetigo and spurious inflammations entailing voluminous adenopathies. In their youth they are in danger of falling a prey to osseous or articular tuberculosis, which soon generalizes and prematurely ends their lives. In this way the races of degenerates disappear according to the great laws of natural selection.

The disorders of nutrition determined by *chronic intoxications* frequently manifest their influence in the offspring. Children of dipsomaniacs are badly developed and present numerous stigmata. Their size is below the average. The statistics published by the recruiting stations show for each department an almost perfect parallelism between the diminution of the size of the recruits and the quantity of alcohol absorbed. The evolutive disorder may go so far that young men eighteen or twenty years old may be no more developed than children of fourteen or fifteen. The pilous system is rudimentary and the sexual organs are small. In addition to this infantilism better marked malformations may exist, such as cranial or facial asymmetry, porencephalia, hydrocephalia, and neurogliar sclerosis of the nervous centres.

If we pass from the anatomical study to that of the functions, we shall note numerous disturbances of the nervous system. Anæsthetic and hyperæsthetic spots are observed, as well as exaggerated reflexes. Sleep may be disturbed by nightmares, terrors, and frequently by urinary incontinence.

The disposition of the subject is sad, morose, and sensibility is exaggerated. Intelligence is often precocious, and may seem to announce great intellectual qualities. But soon an arrest takes place, or, at least, a lack of equilibrium, weakness of attention and of will, and some oddities of ideas and behaviour will be noticeable. At times, however, a few aptitudes persist, particularly artistic talents. But even in this case the asthenia of the nervous system expresses itself in a deficient moral sense and in bad and irresistible impulses. Among these vicious impulses dipsomania takes a distinct place. It is frequently said that an abuse of liquors leads to alcoholism; but it is generally the reverse which is true. The first excess is only the occasion which sets in motion a predisposed nervous system.

We must hasten to add that heredity is not inevitable. When the son of an alcoholic is preserved from the influence of occasional causes, the development of dipsomania is retarded or even definitely prevented. Unfortunately, the occasions are often almost unavoidable for the young man in the workshop, in the army, and, above all, in the colonies. Nothing will henceforth stop the person who, following his parents, has begun to drink.

What we have just said of dipsomania also applies to misdemeanours, thefts, or crimes. Of late, moralists have justly insisted upon the increase of child criminality. If antecedents are looked for, it is found that most young criminals are sons of degenerates, and particularly of alcoholics. On the slightest provocation the nervous system reveals these innate aptitudes.

Several other less serious disturbances have the same pathogenesis. Convulsions, which are too readily looked upon by parents as common reactions, take place chiefly in tainted children on account of a parasite, an intestinal worm, or an infection like pneumonia. In certain instances the disorder may become more serious. The infection may localize itself in the predisposed nervous system, particularly in the spinal cord, and provoke an infantile paralysis. In other cases an intercurrent cause may determine the appearance of a neurosis, of hysteria, and especially of epilepsy. In 80 out of 100 cases epileptics are born of parents tainted with alcoholism.

The other chronic intoxications are equally apt to give rise to morbid disturbances in the descendants. First of all, saturnism may be cited. When the mother is poisoned, abortion is the result most frequently observed. When it is the father, accidents are not less frequent, as is shown by the following figures, taken from C. Paul: Out of a total of 141 cases, there were 82 abortions, 4 premature births, and 5 stillborn children. Of the 50 children born alive, 20 died in the course of a year, 15 died between the first and the third year, and 14 were still living. When they survive, such children suffer from various morbid manifestations already referred to: frequent convulsions on the slightest cause, various degenerations, and serious nervous disorders, such as epilepsy, imbecility, idiocy, etc.

We need not insist upon the other intoxications. Concerning carbonic oxide, mercury, and morphine, we could repeat what we have said about alcohol and lead; but, of whatever nature the intoxication be, when degeneration reaches a certain degree, sterility supervenes. Thus inferior and defective races disappear.

HEREDITY IN INFECTIOUS DISEASES.—The study of intoxications leads us quite naturally to that of infections, since it is through their toxic products that the microbes act.

We have already sketched the history of intrauterine infections; we have shown how microbes pass from the mother to the fœtus through the placenta and how, less frequently, the infection is communicated by the father.

In the cases where the pathogenic agent does not traverse the placenta, the product may present a series of accidents called *para-infectious*, studied particularly in *syphilis*. It may be, first, a special cachexia, sometimes causing the death of the fœtus. Hence, the frequency of abortions. If it comes into the world at all, the child is weak and has a bad constitution. It develops slowly, teething is retarded and defective; at times the number of teeth is below the normal, at other times it is higher; a supernumerary tooth introduces itself between the two superior incisors. The teeth are dwarfed, striated, eroded; the superior median incisors frequently suffer a particular deformation described by Hutchinson—namely, a notched depression in the cutting margin of the teeth.

The bones are poor in lime salts; hence their deformations, which are especially noticeable in the frontal bones and the tibiæ. Parrot even maintained that syphilis is the great cause of rickets. It may well be that it predisposes to digestive disturbances, upon which the development of this morbid state apparently depends.

Other parts of the organism are also affected: keratitis and deafness frequently exist. With the dental alterations they constitute the triad of Hutchinson. The bodily and intellectual development is slow, infantilism is frequent, the genitals remain rudimentary, puberty is retarded, intelligence is weak, sometimes nil, and convulsions are frequent. At times matters go even further. Besides the various stigmata just named, congenital malformations may be observed, such as spina bifida, harelip, hydrocephalus, or microcephalus.

It is chiefly maternal heredity which engenders the disturbances just indicated. Paternal influence shows itself preferably in abortion. Out of 103 cases of pregnancy due to male syphilitics, only 19 children survived; 43 of them died in early infancy, and 41 died *in utero* or were aborted.

But we may take comfort in the fact that the pernicious effect of syphilis slowly decreases and ultimately disappears. It is generally admitted that after a treatment of two years there are already some chances of having healthy children. After three years, it is almost the rule.

Children of *tubercular* parents do not fare much better than those of syphilitics. They particularly present thoracic malformations, as if the respiratory disorders of the parents reacted upon the development of their lungs. Their respiratory capacity is below the average,

and their lungs are often affected with emphysema—an alteration which Virchow has long considered as congenital. It is probably on account of this pulmonary dystrophia that the thoracic cavity develops badly. The chest is narrow, lacking in depth, the shoulder blades project, and the respiratory muscles are small.

Finally, in these, as in all children born of diseased parents, the following additional stigmata may be observed: Slow teething, insufficient ossification, infantilism, defective development of the genital organs, of the circulatory apparatus, and particularly of the aorta. In the opinion of some authors, this last defect explains the frequency of chlorosis. Hanot has insisted on the lobulation of the liver and of the kidneys.

When the parental infections do not go so far as to cause stigmata or bodily lesions, they frequently impart particular nutritive habits to the cells of the child and give to their humours a particular composition. It is in this way that *predispositions* and *familiar immunities* are produced.

If we leave aside tuberculosis, which we have already considered, we may mention a large number of infections of remarkably frequent occurrence in certain families. Such is the case in diphtheria, and especially in erysipelas, which in 13 out of 100 cases is a family disease. The child probably receives from one of its parents a particular mode of nutrition, rendering its organism favourable to the culture of a special microbe. Consequently these cases must not be regarded as similar to those in which one of the parents is diseased and produces a child incapable of offering resistance to the first microbe it chances to meet. In the former case, the predisposition is specific; in the latter, it is general.

Conversely, heredity explains certain immunities. It is justly said that infections work havoc when they reach a population for the first time. Such was the case with measles in the Faroe and Fiji Islands. If these diseases are innocent in Europe, it is because our ancestors who had them have transmitted to us a part of the immunity they acquired. But these facts have slowly been evolved through long ages. It is relatively difficult to understand their mechanism. Let us rather consider what takes place when immunity has just been acquired by the parents.

The first question is: What is the respective rôle of the two generators? Let us begin with the simplest case: The mother suffers during gestation from an infectious disease. We may admit that the protective substances formed in her system traverse the placenta and confer a certain degree of passive immunity upon the product. Thus, a child born of a mother who has had smallpox during pregnancy has

acquired immunity from this disease. If a woman be vaccinated just before the end of gestation the child will for a certain length of time resist the smallpox virus; but this immunity is feebly marked and does not last; moreover, it is not a constant result. Analogous facts observed upon animals inoculated for rot, symptomatic anthrax, or hydrophobia complete the proof of the existence of ovular inoculation (Toussaint), but they also demonstrate that the immunity thus acquired is not well marked and is of short duration.

The second problem is more interesting. It can be formulated as follows: Is it possible for the generators to transmit the immunity acquired by them against an infectious disease?

Ehrlich, who was the first to study this question experimentally, inoculated a certain number of animals against tetanus, abrine, or ricine. On mating these animals with noninoculated ones, he discovered that the inoculated females always transmitted a certain degree of immunity to their offspring, while the influence of the male was nil. Wernicke's researches on diphtheria have confirmed this conclusion.

Nevertheless, Tizzoni and Centanni and Charrin and Gley hold that immunity may have a paternal origin, although, according to them, this is rarely the case. Vaillard, who again took up the question, making use of animals vaccinated for tetanus, cholera, and anthrax, reached the same conclusions as Ehrlich—namely, the father exerts no influence, but the mother transmits a slight immunity, which may be increased by suckling.

Three theories have been offered to explain these facts: One of them is advanced by Duclaux and supported by Arloing, Charrin, and Gley. It is the cellular theory, the only acceptable one if it be admitted that the father may transmit immunity. It supposes that under the influence of the disease the cells receive a new orientation, which persists in the descendants.

If, following Ehrlich, Wernicke, and Vaillard, the paternal influence be rejected, we are quite naturally led to admit that immunity in the child depends upon the passage through the placenta of protective substances produced in the maternal organism. The immunity of the fœtus is of shorter duration than that of the mother, because it is a passive immunity, a simple impregnation.

The theory of Vaillard is related to the preceding: The fœtus is supposed to receive the soluble products, but, instead of simply soaking the cells, they act as a stimulant upon the phagocytes. This is to extend to the problems of heredity the theories of Metchnikoff concerning the mechanism of immunity.

In conclusion, our study of heredity in cases of infection shows that six eventualities are possible:

1. The microbe, coming from the mother, traverses the placenta and causes in the fœtus a disease at times more serious than in the mother (pneumonia, typhoid fever, sometimes syphilis); at times similar (smallpox), but in some cases presenting special localizations (syphilis); at times different (typhoid fever, anthrax). The manifestations are generally immediate, but they may be tardy (syphilis, perhaps tuberculosis).

2. The microbe comes from the father and invades the organism of the fœtus, the mother remaining intact; but she may acquire immunity against the infection afflicting the offspring (syphilis).

3. The microbe does not reach the fœtus; but the child suffers from dystrophic disorders manifesting themselves in malformations, stigmata, degenerations, and infantilism.

4. The child seems normal, but it has received from its mother (or from its father?) an immunity, generally not well marked and of short duration.

5. The child receives from its father, or from its mother, a particular nutrition, which predisposes it to certain infections.

6. The child is in no wise influenced by the infection of its parents.

Thus every contingency may become a reality, from an infection leading to speedy death to the total absence of impregnation.

The very important history of the heredity of neoplasms, and of cancer in particular, might find place in the study of chronic infections. The question will be dealt with in the chapter devoted to tumours.

NERVOUS HEREDITY.—We have several times had to bring in the influence of nervous heredity. We have seen in connection with intoxications and infections that disorders caused by external agents could be transmitted to successive generations and manifest themselves in degenerations, disturbances, or lesions affecting chiefly the nervous system. Chronic alcoholism, saturnism, mercurialism, morphinism, and, among the infections, syphilis and tuberculosis, exercise a pernicious influence, which we have already considered. An acute intoxication may at times produce the same disturbances. For example, drunkenness at the moment of conception is often a cause of degeneration. To it belongs a large share in the etiology of epilepsy.

Moral impressions often exercise a marked effect upon the nervous system of children. When conception or gestation takes place under the depressing influence of mourning, of annoyances, or during the great emotions aroused by public calamities, the children are almost inevitably condemned to nervous degeneration. A striking illustration is supplied by the case of the young men born during the siege of Paris or the Commune.

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The age of the parents may also have a similar effect. In this regard both old age and immaturity exert an influence equally pernicious. If the parents are too young, the first children will be degenerates; those coming later on and conceived during full maturity will be normal. Then, as the years go by, the parents grow weak and bring forth children much inferior to their older brothers. It is conceivable that, under such circumstances, the children of the same family do not necessarily resemble each other, especially if we remember that most of the causes of dejection, sorrows, terrors, as well as diseases, exert only a passing influence. They affect one of the children, not all. Although it is theoretically easy to perceive the influence due to these various causes, in practice it is a much harder task. It is, therefore, no wonder if the ineluctable law determining heredity frequently escapes notice.

We must also remember that the nervous manifestations grow worse in the descendants, and that, after a few generations, they become serious enough to entail sterility. This has very justly been called *progressive morbid heredity.*

The inherited nervous manifestations are not always identical with those of the parents, not even always analogous. Three cases present themselves: At times there is perfect similarity. This is what frequently happens as regards hysteria. At times the manifestations are only homologous; the disturbances differ in their expression, but they are all disturbances of the nervous system. In other cases the symptoms seem quite different and their affiliation can not be understood except by taking into account the idea of diathesis. For instance, the case may be one of an arthritic whose parents, being gouty or diabetic, have had neuropathic children. These transformations are not too much to be wondered at. Long ago clinical experience taught us that nervous disorders are frequent in all arthritics. In this connection we may mention hypochondria, the insanity of gout, diabetic pseudo-tabes, and the insanity of rheumatism. It is one of these accessory and, in a way, superadded disorders in the parents which becomes predominant in the next generation.

In order that the nervous manifestations to which heredity predisposes may come to light, *an occasional cause* must intervene. This is, by the way, a notion of capital importance from a prophylactic standpoint. The disturbances become apparent on the occasion of a traumatism, an infection, an excess, or a moral shock. It is the first drinking bout which is the starting point of dipsomania, and it is a common infection which, as it causes convulsions or delirium, reveals the congenital neuropathy. It may happen that these manifestations begin earlier in the children than in the parents. A father whose

neuropathic aptitudes do not reveal themselves until late in life may have a child who, from his first months, has convulsions. In this case hereditary influence would be manifested only at a later date, and if the father dies too early—i. e., before having brought to light the taints which slumbered in his organism—the problem remains unsolved and the child's disorders will seem to be spontaneous.

Although the parents generally communicate to their descendants a mere aptitude, they may at times transmit to them a true disease, connected, it seems, with an evolutive disorder. It is a kind of *ovular* affection. As an illustration, we may mention the hereditary ataxia of Friedreich, the cerebellar hereditary ataxia of Marie, the progressive myopathy of Landouzy-Dejerine, the disease of Thomsen, the so-called hereditary trembling. These various diseases have in common the following traits: They appear at the same age in the parents and in the children; they occur without any occasional cause, and they reproduce themselves with uniform aspects.

In most cases heredity transmits a certain tendency to nervous manifestations, and to ordinary reactions which occur on the occasion of a traumatism, an insolation, an infection, or an intoxication. Pneumonia, which in children is so often accompanied by cerebral disturbances that an eclamptic and a meningeal form have justly been described, so acts, however, only upon predisposed children. It may be stated that, even in cases where nervous manifestations seem inevitable, their frequency, intensity, and other characters are governed by predisposition. Drunkenness, for instance, is not necessarily accompanied by cerebral accidents. There are men who can absorb great quantities of liquor: their reason remains unaffected; and they suffer from digestive disorders. Others, on the contrary, prepared by their heredity, become delirious at the slightest departure from their ordinary regimen.

What we have said in reference to alcoholic poisoning may be repeated concerning endogenous intoxications. In uræmia, for instance, the manifestations vary so much that three clinical forms of it have been described according as the accidents involve the digestive apparatus, the respiratory apparatus, or the nervous system. It is generally admitted that the variability of the symptoms depends upon the multiplicity of the poisons, and that the manifestations differ according to the substance which accumulates. We accept this conception, but it seems to us that the rôle of hereditary dispositions must be taken into account: The localizations are determined by the state of the organs. Uræmia is only an occasional cause that brings to light morbid dispositions which until then had remained latent.

In a certain number of cases the nervous taint explains the devel-

opment of the disorders which appear during or after a disease and persist for a very long time. This is the case with chorea, hysteria, epilepsy, and paralysis agitans. Chorea, for instance, occurs frequently after an attack of rheumatism, but only when the subject is hereditarily predisposed to neuropathia. The same is true of the other neuroses. The expressions traumatic hysteria, infectious hysteria, used quite frequently, point to this double tendency. It is not that hysteria differs in its symptoms, for they are always the same; but it is brought about by a number of occasional causes, all of which act on predisposed subjects.

It would be easy to add analogous considerations with regard to all infections which become localized in the nervous system, whether it be meningeal tuberculosis, cerebral rheumatism, infantile paralysis, locotomor ataxia, or general paralysis. In the last two cases the rôle of syphilis, the influence of which is undeniable, must be supplemented by the effect of hereditary predisposition, which alone explains the localization.

It is not only in pathology, but also in *psychology* and *sociology*, that nervous heredity offers an interesting subject of study. Intellectual aptitudes are transmitted for several generations. There are on record families of scientists, of writers, of musicians, and of painters. Oftentimes a quality is exaggerated, and, becoming predominant, explains the appearance of superior individuals. The power of attention, the persistence of ideas, when intensified in the descendants, may culminate in a genius. It is also by an insensible increase of the familiar qualities that the aptitude for cerebral work develops in civilized races, and mental overtaxation becomes possible.

It is quite certain that it is not every one who can indulge in mental overwork. In order to do this one must have been prepared by heredity.

Reciprocally, a slight disorder may deviate and grow. The tendency to fixed ideas may breed melancholia. Cerebral activity may be excessive and excite in the child the most varied neuroses. As defects increase with age, it frequently happens that children are the more degenerate the later they have been conceived. Here is an observation which, in this connection, is highly instructive.

A woman in whom the neurotic tendency was at first little marked, but had grown with age, had an attack of influenza when fifty-four years old. The nervous symptoms at that time assumed a more serious character; she imagined that her soul left her body and sat down by her side. This woman had married an intelligent and well-balanced man, and had four children. The eldest is thirty years of age; she is a woman of a superior intelligence, but marked as a degenerate by two

physical stigmata: facial asymmetry and strabismus. Although now married for eight years, she has no children. Her brother, twenty-six years old, has a bright but childish intelligence; he busies himself with table tipping and spirit communications. The third one, nineteen years of age, is a somnambulist. The fourth, sixteen years old, is a hypochondriac with morbid impulses; he several times tried to commit suicide, and one day attempted striking one of his brothers with a knife.

In this family the accidents have gone on increasing as the mother has grown older. The last of her children is in a condition bordering upon insanity.

The statement that *insanity* is often hereditary is a commonplace truth. According to the statistics of Hutchinson, it is hereditary in the proportion of 22.6 per cent.

Consequently here, as everywhere else, heredity is not inevitable. It is more frequent when the mother is insane, and it decreases in frequency as the cerebral disorders become manifest in the parents after the birth of the children.

Aside from similar heredity, the influence of the conditions in which the parents are found must be taken into account. Chronic alcoholism and drunkenness at the time of conception play the same part as the other defects of the nervous system. To these factors must be added two others: Overwork on the one hand, and arthritism on the other, contribute their part and account for the growth of the number of insane persons in the civilized races. The increasing complications of life, exacerbation of discomfitures and disappointments, overtaxation of mental powers, and predominance of the nervous system, sufficiently explain the progress of mental disorders.

Thus endowed with an hereditary predisposition, the individual waits for an occasional cause and then succumbs to insanity. The breaking down may happen at the great periods of growth. There is an insanity of puberty and, in women, an insanity of the menopause. Or the occasion may be childbirth, an external influence, a nervous shock, a violent moral impression, an intoxication, or infection. It must be said, however, that the interpretation of the disorder is not always easy. Alcoholic or venereal excesses and overwork are very frequently not the cause of the mental disease, but represent only the first symptoms. This is unquestionably the case in general paralysis, in which the initial manifestations have often been mistaken for the starting point of the disease.

If heredity is frequent in insanity, it is certainly not inevitable. In certain forms, as in chronic delirium, it is constantly found; while it is quite rare in general paralysis. It has even been noticed that

the sons of general paralytics are frequently endowed with a high order of intelligence and sometimes with genius.

Genius, Insanity, and Crime.—In a book which created a sensation, Moreau de Tours defined genius as a form of neurosis. Although this view can not be accepted, it must, at any rate, be admitted that cases of genius and insanity and of genius and neurosis are frequently found in the same family. It is also well established that a large number of highly gifted men present stigmata which, according to the happy appellation of M. Magnan, make of them superior degenerates. To speak but of the dead, it suffices to mention Socrates talking to his spirit, Pascal terrified by hallucinations, and J. J. Rousseau, a hypochondriac with secret vices (Confessions). The study of the psychic status of superior persons reveals an exaggerated or perverted sensibility, the absence of practical sense, queer superstitions and accidents bordering upon pathology, manias or phobias. This fact is becoming a matter of common observation, and has suggested the interesting researches of M. Toulouse on the mental state and the signs of degeneration of our most illustrious contemporaries.

Reciprocally, an insane person can have sparks of genius. The beginning of general paralysis affords abundant illustrations of this peculiarity. Tradition understood the relation existing between these two extremes and joined them in the term " poetical delirium." How many superior men, artists, musicians, and scientists, are looked upon as " cracked " by their neighbours! How many men called lunatics by their contemporaries hold the rank of geniuses in the eye of posterity! This is because geniuses and lunatics differ from the sensible man in the same particular. Their ideas are opposed to those of the majority. It is this that makes the great difference between a talented man and a genius: the former continues and completes the ideas current about him; the latter departs from them and conceives different thoughts. It is no easy matter to determine when an idea springs from genius and when from insanity. It may even happen that they are analogous in both cases. Specialization in predisposed persons depends upon external circumstances.

It has sometimes been said that relations exist between genius, insanity, and crime. In this form the statement is unacceptable. There are affinities between genius and insanity on the one hand, and insanity and crime on the other; but there are none between criminality and genius. Men of genius are superior degenerates, criminals are inferior degenerates. For the sake of greater clearness, let us suppose an angle whose sides extend to an infinite distance: at the apex we place insanity, on the ascending side genius, and on the descending side crime. Despite the point possessed in common by both

psychic states, they evidently diverge more and more from each other; their differences increase as the man of genius ascends and as the criminal sinks.

The relationship between insanity and crime is so evident that the question of responsibility rises constantly. Many delinquents who formerly would unquestionably have been punished are to-day confined in asylums. The differentiation is, it hardly need be said, very difficult to make, and the idea of partial responsibility, so often applied, serves only to indicate the existence of numerous transitions connecting insanity and crime. The differentiation can be made from two points of view. The public considers any crime as the work of a lunatic, and, as a rule, any act the motive of which can not be understood. The physician must judge differently; he must determine the bodily condition of the accused, seek for stigmata, reconstruct his past, discover his personal, and especially his hereditary, antecedents.

In studying the families of criminals, we sometimes find direct heredity (25 per cent of youthful criminals are born of criminal parents), and sometimes indirect heredity—that is, neuroses, degenerations, mental derangements, and alcoholism. As a rule, child criminals belong to families of alcoholics.

If we turn from the family to the individual, we frequently observe stigmata of degeneration. The criminal is liable to irrational fits of anger, to night terrors; and at times the disorders are more severe. The frequency of insanity in workhouses and prisons is to be explained not by the peculiar circumstances under which the prisoner lives, but by his hereditary predispositions. Finally, in certain cases, the impulsive nature of the crime is tardily brought into evidence by the occurrence of an epileptic fit, which makes it possible to properly determine the moral responsibility of the subject.

Heredity is no more inevitable here than elsewhere; occasional causes, as is always the case, play a very important part. If the individual, predisposed by heredity, is brought up among honest people, his chances of not straying from the straight path are good. How many people have remained virtuous for the want of an occasional cause! Consider from this point of view the influence exercised by the great social perturbations. Reread, in Thucydides, the story of the Athenian plague or review the history of the more recent great revolutions; it is always the same picture; always the same licentiousness, hatred, violence, and murder. It is a particular state, perhaps a return to an ancestral condition, at any rate, a retrogressive movement, which is produced when the fear of punishment grows weak and when social hypocrisy is done away with. Contagion propagates the disorder, but it reaches those only who carry within them a latent predisposition.

If, on the other hand, criminality, as well as insanity, increases with civilization, it is because the growing complexity of life breeds overtaxation, and requires a new stimulation which seems to be favoured by the use of alcoholic beverages. Heredity expresses itself under these circumstances in an inability for sustained effort, which is the great cause of criminality.

The facts above stated in a summary way appear conclusive when viewed in their entirety. A close relationship must be admitted to exist between crime and insanity. These two conditions are separated only by our social prejudices.

Let us hasten to add that the conclusions to which we are led by an impartial consideration of the facts in no way affect the right of repression; they do no more than change the aspect of the question. The right of punishment must be looked upon as a right of defence.

Physical Stigmata of Degeneration.—Can criminal hereditary predispositions be recognised by means of particular bodily characteristics? According to the theory of Lombroso, who answers this question in the affirmative, the born criminal presents various stigmata which bring him nearer to primitive man. The stigmata are less frequently observed in man than in woman, although she commits fewer crimes. Lombroso meets this objection by the statement that in woman prostitution is the equivalent of crime; as a matter of fact, associations of criminals and of prostitutes are of frequent occurrence. Equally abnormal, these people come together just as other degenerates do. For it seems well established that the various stigmata enumerated by the Italian school do not characterize the tendency to criminality, but simply the degeneration of the race; they are found in degenerates of all kinds.

The stigmata of degeneration are extremely numerous. We shall limit ourselves to the mention of a few of them: Deformation of the cranium and of the face, their asymmetry, existence of abnormal sutures, protrusion of the superior or of the inferior maxillary, deepening of the palate, irregularities in the development of the teeth and their speedy decay, harelip, hollow thorax, absence of one or of two pectorals, short fingers, lumbar hypertrichosis, exaggerated development of the pilous system in woman and the reverse in man, imperfect development of the genitals, delayed descent of the testicles, bipartite or imperforate vagina. As regards the organs of sense, strabismus, pigmentary choroiditis, daltonism, deformities of the iris, deaf-mutism, anomalous development of the ears, adhesion of the lobe, absence of the marginal fold, and anomalies of the helix, which in some cases joins the antihelix; among the nervous disorders, stammering, tics, etc.

If we consider the intellectual development, we find all imaginable types. At the foot of the ladder, idiocy; the cerebral functions are so reduced that we may consider the subject as a mere medullary being. Nevertheless, one faculty may persist: idiots have been known who were excellent musicians or astonishing calculators. A little higher we find imbecility, and still higher mental debility. Above these we find very intelligent, even superior, persons, but they are in some way defective; they are odd, eccentric, gifted at times with a partial superiority, but their character betrays asthenia: defect of judgment, inability to look after themselves in life. There are men of genius whose mental degeneration is expressed by the absence of practical common sense, or by some little defect which astonishes, or by some fantastic mania, or incomprehensible phobia.

Every degenerate, whether superior or inferior, whether bordering upon genius, insanity, or crime, very frequently shows an invincible tendency to suicide. At times this is the only stigma, or at least the most apparent one. They sometimes use childish means, but generally they repeat the attempt with increasing earnestness, and generally succeed in destroying their lives.

This tendency to suicide may be transmitted, and, curiously enough, each member of the same family uses the same means and at the same age. Hammond relates the case of a man who, at thirty-five, killed himself in a bath by cutting his throat with a razor. He had two sons who committed suicide at the same age and in the same way. One of them had a daughter who killed herself at thirty-four, and her son put an end to his life when thirty-one years of age.

The considerations we have presented concerning nervous heredity directly suggest practical applications. Prophylaxis may prevent the development of the manifestations to which the child is predisposed. As above stated, an occasion is required to determine the occurrence of the accidents. Consequently, the child should be removed from his family; and this becomes an imperative duty when the parents are alcoholics. We have shown that the first intoxication is the starting point of dipsomania. It is here that the temperance societies are useful. We must remember that coercion in any form—punishment, intimidation, or repression—never succeed. The effective treatment is to place the child in the country in the family of honest and quiet people. Moral guidance saves a large number of predisposed subjects, and even a few delinquents. We do not speak of the hardened cases; they are incorrigible.

It is in this manner that effects of heredity may be successfully antagonized, effects which—we can not repeat it too often—do not rest upon the race as an unavoidable fatality.

It is not impossible for a man to escape from his inheritance; it is even possible for him to differ entirely from his ancestors or collaterals. There are cases which appear to defy all our laws and theories. Occasionally a genius, a lunatic, or a criminal appears altogether unexpectedly; nothing of his character precedes or follows him. No doubt the anomaly is only an apparent one, but its causation escapes detection. Perhaps we have failed to take notice of a particular influence that has been in action. It is perhaps a return to an ancestral type, as in the curious case reported by Darwin in which a pigeon of a peculiar colour appears suddenly in a race apparently fixed by long selection.

CONCLUSION.—The study of heredity completes the history of etiology. If the causes of diseases must always be looked for outside of the organism, the modes of its reactions are governed by predisposition, aptitude, and resistance transmitted by the parents. The functional modifications accidentally brought about are communicated to the offspring and are often exaggerated in successive generations. According as the attendant circumstances are favourable or detrimental, the family, the race, or the species will show a corresponding improvement or deterioration.

By an abuse of expression, it is often asserted that the affections of the organs—the heart, the liver, the kidneys, and the nervous system—are hereditary. What is transmitted in most cases is a functional disturbance—i. e., a simple disposition, which becomes apparent only under the influence of exciting causes.

Children born of parents suffering from cardiac, hepatic, or pulmonary disorders or from Bright's disease are more likely than others to develop lesions of the heart, liver, lungs, or kidneys. But an occasion will be required in order to make actual the inherited tendency; a new influence, an intoxication, an infection, or an anomalous nervous reaction will have to interfere in order that the organ be affected. It is in this way that the heredity of visceropathies must be understood. It is even probable that what in many cases appears to be hereditary pulmonary tuberculosis is due rather to the fact that the offspring of tubercular subjects suffer from insufficient respiratory activity, their breathing capacity being below the normal.

Heredity must not be mistaken for "*innateness.*" The latter expression designates those cases in which the child comes to life presenting certain morbid aptitudes, the point of departure of which is to be found in some accidental causes having exerted their influence directly or indirectly during conception or gestation.

Innateness is the conclusion of fœtal pathology, while heredity is a chapter of the pathology of the species. Innateness results from ex-

ternal causes which have acted upon the fœtus through the enveloping membranes. More frequently it arises from toxic or infectious agents transmitted through the placenta. At times it proceeds simply from bodily or psychic disorders in the parents. A well-constituted person generating a child during convalescence from an intercurrent disease, a woman under depressing influences during pregnancy, would produce an offspring with a particular innateness. It might exhibit nutritive disorders or stigmata of degeneration; it would be predisposed to neuropathies and easily contract infections. The morbid influence having acted upon cells that are young, and, so to speak, malleable, would leave an indelible imprint. The disorder would be permanent in the child, even though temporary in the parents.

Innateness frequently results from causes so slight that they escape notice. If the great laws of heredity at times seem to fail, it is because we do not always perceive the circumstances modifying their action.

In cases of organic as well as of nervous affections, it is a predisposition which is transmitted in the majority of instances. Hence, the importance of prophylaxis and education.

Hereditary taints are only too often aggravated by education. The sons of neuropathic or alcoholic parents are incited by the examples they see in their families to deeds which seal their doom. If, instead, they were placed from early youth under the care of persons able to start them in a good direction, the effects of heredity would be resisted, and even completely overcome.

Unfortunately, it is but seldom that education is used for this purpose. Moreover, its influence may be insufficient. If that be the case, the disorders of the parents will go on increasing. It is in this manner that pathological families are created. If to this be added the fact that the same defects are frequent in the same classes, it is easy to see how marriages between persons having the same aptitudes will still more tend to magnify the hereditary disorders. On the other hand, social selection frequently brings about the survival of the weak and degenerate. It then seems to supplant natural selection, but it does so only temporarily. Infecundity or increasing debility brings about the extinction of degenerates. We are thus brought back to the great laws regulating the whole evolution, and we are led to look upon social selection as a mere chapter of natural selection, sociology being simply a chapter of biology.

As it transmits and fixes certain characteristics, heredity explains the evolution of races, their diverse aspects at different epochs and in various countries, and by this very reason accounts for their pathological variations. Diseases are not the same all over the globe; they

differ also according to the period. The variations of pathology in time and in space find their explanation in the incessant changes occurring in the cosmic agents, in the animate beings, and notably in the human species. This is the reason why the diseases we observe differ from those observed by our fathers, just as they differ from those which will come to the notice of our descendants.

We can now clearly understand the variability of clinical types. The various localizations taking place during infections and intoxications, the diverse nervous reactions happening on the occasion of a traumatism, are not the work of chance. They everywhere and always proceed from numerous causes which have influenced the subject or his generators.

If the varied circumstances intervening before and after birth could be traced out, if precise information regarding heredity and innateness could be obtained, and if the external causes playing upon the fœtus could be known, the future of each individual could be foreseen, and its physiological, pathological, and moral history written out in advance. For it is quite certain that as all the activities of living beings are nothing more than reactions provoked by external agents, they must all be interrelated just as systematically as the other cosmic phenomena. Only it is impossible to discern the innumerable intervening causes. It is for this reason that the freedom of living beings has been so long admitted. Our belief in morbid spontaneity, just as our belief in free will, is grounded upon no other foundation than an incomplete knowledge of the numerous causes acting upon us.

CHAPTER XIV

INFLAMMATION

Definition—Part played by local lesion—Mode of formation of inflammatory foci—
Active congestion—Diapedesis—Liquid exudation—Modification of the fixed
cells—Chemical study of serous exudates—Principal inflammatory processes—
Pseudo-membranous processes—Suppuration—Chemical and histological con-
stitution of pus—Principal pyogenic agents—Microbic and nonmicrobic suppu-
rations—Transformation of pus—Symptoms and course of purulent collections
—Gangrene—Part played by microbes—Importance of accessory causes—Part
played by circulatory, nervous, and dystrophic disturbances—Principal ana-
tomical and clinical varieties of gangrene—Infectious nodes—Tubercles—Ana-
tomical varieties and histogenesis of tubercles—Principal clinical forms of
human tuberculosis—Tuberculosis of animals—Unity of tuberculosis—Pseudo-
tubercles: their varieties and importance.

Definition.—When a pathogenic cause acts upon any point of the
organism, it occasions two orders of responsive manifestations, some
local and others general. Local reactions are due to cellular modifica-
tions induced at the point of application of the cause, and to modifica-
tions of a reflex order. General reactions are referable to nervous
influences or to the absorption of toxines.

Let us consider, for example, a mechanical agent which has pro-
duced a cut: The edges of the wound are slightly separated, and the
open vessels are bleeding. The first reactions will arrest the hemor-
rhage; on the one hand, the calibre of the vessels will contract in
consequence of the direct excitation of the nonstriated muscular fibres
entering into the structure of their walls, and on the other hand as
the result of a reflex constriction. The blood, flowing with less force,
will coagulate; fibrine will be formed, and its effect will be to occlude
the vessel, to assure hemostasis, and to unite the edges of the wound,
and then serve as nutrition and as a guide to cells which will insure
reparation. The second act then begins. The cellular elements lining
the solution of continuity begin to proliferate and form a cicatrix. At
the same time leucocytes enter the field, some to take part in the for-
mation of tissues, others to carry away the dead cells and to clear up
the ground.

When a toxic substance is deposited upon the skin, two results are possible: In some cases the poison is absorbed without giving rise to any local irritation; in others, a reactionary lesion is produced at the point of its introduction. The poison has destroyed the cells, and these cause a vaso-dilatation, a serous exudation, and œdema by reflex action. Thus formed, the local lesion dilutes the toxine, prevents its absorption, and in this way protects the organism.

Let us now suppose that the process is due to a microbe—for example, a pus coccus. When it finds itself in favourable conditions, it develops. If it only acted mechanically, it might multiply and produce a voluminous colony without exciting any general reaction. But, at the same time that it multiplies, it engenders toxines which cause the death of cells with which they come in contact. Thus is produced a necrobiotic zone, which is later surrounded by a proliferative zone. Around the cells that have been killed the elements develop in such a manner as to circumscribe the infection, to struggle against the microbe, and to replace the destroyed parts. Coincidently with the occurrence of these first phenomena, the nervous terminations are aroused by the microbic toxines and by the dead cells. Their excitation gives rise to a series of reflex acts which, ending in the active dilatation of the vessels at the invaded point, are followed by migration of leucocytes and the formation of a serous exudate. In this way a local lesion is produced.

In order that these various phenomena may be produced, the microbe must possess a virulence of medium intensity. If it is inoffensive, it can not multiply, and is soon destroyed by the cells. The local lesion does not appear, and the infection is aborted. If the microbe is too powerful, it secretes a series of substances which prevent vaso-dilatation, the issue of plasma and leucocytes. The local lesion is again absent, but general infection is at once produced.

The local lesion then represents a fortunate process, and is a barrier opposed to invasion. Its effect is to circumscribe infection and prevent extension and generalization of the process. It may, however, have its disadvantages. In certain cases the organism disturbed by the arrival of the microbe mobilizes more forces than are required and provokes a local lesion liable to become dangerous. Thus, in the larynx, under the influence of an infection, as in the case of a burn, œdema of the glottis may be produced which will cause death mechanically. In the lung, active congestion caused by a microbe may bring about grave accidents. The animal organism is not capable of proportioning its intervention to the action of the cause. Hence it is that, for a little tubercle situated under the pleura, it will secrete three or four pounds of serous liquid. This exudation will hinder the

development of tuberculosis by the compression it exerts, but its abundance will produce accidents, and if timely thoracentesis be not resorted to it will in some cases cause death.

The disproportion between cause and effect is well brought to light by a very ingenious experiment of Gamaléia. Two rabbits were taken and their cornea slightly cauterized; one of them was kept as a control, and soon presented a white spot at the point of traumatism. In the other the development of the inflammatory phenomenon was prevented by injecting into the veins strong salt water. The healing was obtained without a cicatrix. It is easy to understand the importance of these facts in therapeutics, for we possess the means of stimulating or preventing reactions, and notably congestive phenomena.

Whether there be a local lesion or not, microbes can pass into the blood. This liquid, however, is not favourable for them, so they rapidly deposit themselves in the tissues. They develop there, and again secrete their toxines, and thus give origin to secondary foci, whose mechanism is analogous to that presiding over the formation of the primitive focus.

These two types of foci, primary and secondary, constitute the process described under the name *inflammation*.

There is no term in medical language that has been more variously defined, no process that has been more diversely interpreted. Among the numerous conceptions that have been put forth three deserve to be mentioned:

The first, by order of date, is that of Virchow. According to the celebrated pathological anatomist, inflammatory phenomena consist in degenerations and proliferations bearing on the fixed cells of the affected tissues. The vascular changes produced in the morbid foci seemed to him secondary.

Cohnheim's conception was quite different. The vascular modifications were considered by him to be the initial phenomena; the effect of vaso-dilatation was to permit the escape of white blood corpuscles through the vascular walls, according to a process called *diapedesis* (migration).

This conception, based on unassailable experiments, gave occasion to lively discussion. It was of late completed by Metchnikoff, who holds inflammatory reaction to be salutary, as its end is to permit the leucocytes to devour and digest the invading microbes—namely, to fulfil their phagocytic function.

Each of these three theories contains a great amount of truth.

We consider, in fact, that inflammation is "the *ensemble* of reactionary phenomena produced at the irritated points by a pathogenic agent." In most cases the agent is a microbe, but in some it is a

mechanical, a physical, or a chemical agent. Inflammations occasioned by a foreign body, by insolation, or by the application of cantharides are well-known examples.

Mode of Formation of Inflammatory Lesions.—Inflammation is essentially characterized by four orders of phenomena: vascular disorders, which may be wanting in the case of a tissue destitute of vessels, like the cornea; liquid exudations; diapedesis; local cellular alterations.

Congestion and Diapedesis.—The first phenomenon, at least that which first attracts the attention of the observer, is represented by reflex vascular manifestations. The cells, irritated by the toxines, excite the nervous system, and thus cause an active vaso-dilatation. The arterial blood arrives in great quantity, quickly passes through the capillaries, and, in consequence of its abundance and rapidity, reaches the veins, having nearly preserved its characters. The amount of carbonic acid, although exceeding the normal, is diluted in so great a quantity of blood that the liquid remains red in the veins, and, if one is bled, it flows in jerks, by reason of the dilated condition of the arterioles and capillaries.

At this moment the patient is sensible of the congestive phenomena by the heat he experiences, and especially by a sensation of pulsation isochronous to the pulse.

In the second stage the sensation is modified: there is a feeling of heaviness, of swelling, and of painful tension.

In fact, the local condition is changed; the course of the blood current has become slower, and there is produced a set of phenomena which have been experimentally studied by Cohnheim. In order to observe them, one must operate on a frog, draw out an intestinal convolution, and examine the vessels of the mesentery under the microscope. After a transitory stage of initial constriction, they are seen to dilate; then the rapidity of the blood current lessens; the leucocytes, which were at first carried off by the current, come to adhere to the endothelium of the vascular walls. This *margination of leucocytes,* to use an expression of Cohnheim, can not occur in the arteries, for the too rapid current carries on the few cells which try to fix themselves; it takes place in the capillaries, and chiefly in the small veins. Once fixed, the leucocytes change their form, send out processes, which engage between the endothelial cells, separate the walls of the vessel, and thus produce an opening through which they pass out of the circulatory system. This is *diapedesis.* When the leucocytes have passed out of the capillary, the hole that they leave behind them again closes up, but not quickly enough to prevent a few red blood corpuscles from passing into the surrounding tissue.

The leucocytes are not all equally apt to pass out from the vessels by diapedesis. It is especially those that belong to the varieties known as mononuclear and polynuclear neutrophiles that are endowed with the most active movements and emigrate most easily.

The process of diapedesis requires the presence of oxygen, which stimulates the activity and motility of leucocytes. It stops if a vein is compressed—namely, if an accumulation of carbonic acid is produced; conversely, it is accelerated when the flow of arterial blood is favoured. Three orders of experiments demonstrate the reality of this fact. If the streptococcus or erysipelas be inoculated into the ear of two rabbits, and if in one of them the flow of arterial blood be accelerated by cutting off the superior cervical ganglion of the great sympathetic, it will be seen that exudation is more abundant and diapedesis much more intense in the ear deprived of the nerve. On drawing a little drop of the exudation there are found in the operated animal, at the end of three or four hours, forty times as many leucocytes as in the control. This quicker production of œdema and this more rapid arrival of leucocytes render the inflammation much more acute at the outset, but they precipitate its evolution; the erysipelas is healed more quickly and more completely. The results are similar when, instead of exciting a streptococcic inflammation, physical or chemical agents are resorted to; when, for example, the ears of a rabbit are plunged into boiling water, or are rubbed with croton oil.

Another procedure also brings to light the favourable side of active congestion. Filhene inoculated streptococcus in the ear of two rabbits; then, in one of the animals, he surrounded the ear with a small rubber bag in which hot water was circulating. The elevation of temperature favoured congestion and diapedesis and thus hastened the cure.

Finally, as was done by Dr. Carnot, acute congestion may be accelerated by vaso-dilating substances, such as amyl nitrite; the result, however, is still the same.

Although congestion favours the exit of leucocytes, it does not suffice to explain it; nor is the irritation produced by the air—in Cohnheim's experiment a sufficient condition. Repeating the experiment, and taking care to place the frog in sterilized air, Zahn observed vaso-dilatation; but the phenomena did not go any further. Therefore, if diapedesis is produced under other circumstances it is because the white blood corpuscles are excited to emigration by the numerous bacteria that fall upon the peritoneum from the air.

What is more curious is the fact that once out of the vessels the leucocytes do not travel at random. Urged by a mysterious force, they direct themselves toward the place where the microbes are multiplying. It is assumed that they are attracted by substances secreted by the

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bacteria, and by those yielded by the organic cells, which perish in the struggle. These various substances exercise an attraction which has been called *positive chemiotaxis*. When the microbe is very virulent it produces poisons which, unlike the preceding, repel the leucocytes, and are said to possess a *negative chemiotactic* power.

Serous Exudation.—Coincidently with the emigration of the morphological elements an exudation of liquids takes place. The exudations may be attributed to most diverse causes. Sometimes it is a traumatism that determines an often intense œdema in the subcutaneous integuments. More frequently it is physical agents, sunstroke or heat stroke, cold or burning, that excite a serous swelling. A good many chemical agents act similarly. The action of slight caustics or energetic revulsives is well known; it suffices to mention the blister of epispastics. As in all other cases, the most numerous and varied illustrations are found in the group of infections. Abundant serous exudations are produced at the point where anthrax is inoculated; also at the seat of and around diphtheritic lesions and in corresponding ganglia. They are also formed under the influence of staphylococcus, and especially of streptococcus. Lastly, it is very common to see in serous membranes exudations referable to a tubercle situated in the neighbourhood.

From a mechanical standpoint, liquid exudations are often divided into two groups, according as they are of inflammatory or chemical origin.

In the latter case some hindrance to the venous circulation is admitted. The fact is undeniable: quite tight compression of a limb is sufficient to cause a serous exudation in the cellular tissue. But, in order to produce this phenomenon, the constriction must be brought to bear on all the vessels; anastomoses are in fact so numerous that the constriction of one vein is followed by no effect. If œdema is produced in certain cases it is because the influence of another factor is added to the mechanical action—for example, a microbic toxine or an active congestion. Ligation of the three principal veins of the ear in a rabbit, for instance, does not provoke œdema unless a few drops of a sterilized culture of a microbe, like *Proteus vulgaris*, be injected at the same time beneath the skin, or unless the superior cervical ganglion of the great sympathetic be severed. In man, a phlebitis, even when it affects a vein of little importance, often causes considerable œdema. The fact is striking in the case of varicose phlebitis; but this is not a mechanical phenomenon, since ligature of the same vessel produces absolutely nothing.

It may be asked, therefore, whether a great number of exudations attributed to mechanical influences are not due to more complex pro-

cesses. It may be questioned whether the œdema occurring in cardiac and Bright's disease patients is not often favoured by the development of the microbes of the skin, which tend to penetrate into the integuments under the influence of malnutrition. The same remark applies to the viscera. It is very probable that pulmonary œdema is often due to the action of external germs, which tend to develop in a lung not sufficiently supplied with blood. The same remarks are applicable to serous membranes. The ascites of cirrhotic patients is not always to be ascribed merely to a circulatory difficulty; it is probable that venous stasis permits the escape of intestinal microbes, which irritate the walls of the portal vein or even of the peritoneal serous membrane. The hydrothorax of cardiac patients seem still more frequently to be referable to bastard pleuro-pulmonary infections. In a word, in order that exudations be produced, it is in most cases necessary that an additional process be established to complete the mechanical action of venous stasis.

The chemical distinctions which it has been attempted to establish between inflammatory and mechanical exudations seem very fragile, since there exist numerous transitions between the results obtained. It is asserted that inflammatory exudations are denser; the areometer shows 1,020 instead of 1,010 to 1,015; they contain more proteid matters, more fibrinogen, and they often coagulate spontaneously. Mechanical exudations, on the contrary, do not coagulate, for they contain little of the cellular elements capable of furnishing the fibrin ferment.

Pleural exudations especially have served for the investigations of chemists. Mehu found notable differences, according as the exudation was inflammatory or mechanical. Here are some figures, borrowed from Halliburton, which give the particulars:

	Pleurisy. (Acute inflammation.)		Hydrothorax. (Torpid inflammation.)	
Density	1,020	–1,023	1,012	–1,016
Proteid matters...............	35	– 52	13	– 25 per 1,000
Fibrine	0.1–	1	0.06–	0.1 "
Globuline	12	– 30	4	– 7 "
Serine	11	– 33	7	– 18 "
Mineral salts	7.3–	9	7.3 –	9 "

These figures show that exudations are never due to simple transudation; they would then have a fixed composition. The mineral salts alone seem to escape by exosmosis, since they do not vary. The organic matters escape by a process of true secretion; it is a question of a vital phenomenon connected with the irritation of endothelium.

But it is also easy to convince one's self that there are not radical differences between the two varieties of transudations. Numerous figures of transition prove that the process is always complex, and that in most cases inflammation is added to mechanical action.

Modifications of the Fixed Cells.—While the various modifications just described are being produced, changes by no means less interesting occur in the cells of inflamed tissues. The endothelia of the vessels swell up; the cells of mesodermic origin—namely, the fixed cells of connective tissue—the clasmatocytes of Ranvier, and even the cells of adipose tissue, return to their embryonal state, recover their round form, and recuperate their motility and contractility.

The proper cells of tissues, the epithelial cells, are more highly developed, and hence more fragile. Many of them perish. Sometimes, as if overwhelmed by the action of toxines, they are from the outset struck by death and undergo *coagulation necrosis*. In other instances they first become hypertrophied; their protoplasm becomes translucent, then atrophies and undergoes granular, hyaline, colloid, vitreous, and fatty degeneration. Those situated around the inflamed zone resist better, and their irritation is expressed by karyokinesis and proliferation.

Evolution of Inflammation.—If the inflammatory phenomena are not too intense, the round cells, of mesodermic origin, tend toward organization; infectious nodules are formed, the most highly developed types of which are represented by tubercles and syphiloma. On the part of epithelial cells are observed nodular formations, adenoma, perhaps also epithelioma. We shall return to this question, which touches the much-disputed problem of relationships between inflammations and neoplasms.

If inflammation is intense the cells are killed. According to the nature of the agent and the condition of the organism, and according to the elements attacked, granulo-fatty degeneration, necrosis, false membrane, in which a tendency toward organization still persists, suppuration, and gangrene are observed.

The *clinical manifestations* of these various anatomical processes are extremely variable. However, in the case of free acute inflammation we observe a certain number of interesting disorders.

These are, first, the four cardinal signs of inflammation—pain, heat, redness, and swelling (*dolor, calor, ruber, tumour*)—which occur at the invaded point. We shall make a complete study of these in connection with suppuration. There is produced at the same time an increased functional activity having for its centre the affected point. On the part of neighbouring glands an increased secretion will be produced. But the liquid is often altered and contains only mucus. In

more intense cases the disturbance is expressed by a reverse phenome-
non—namely, a dryness of the parts, in consequence of arrested
secretion.

In the cases where evolution is favourable, the elements that have
perished are eliminated, thrown out, carried away by wandering cells,
or are destroyed by neighbouring cells. Their disappearance is fol-
lowed by the development of a tissue that will fill up the empty place.
This is sclerotic tissue, veritable cicatricial tissue. As in all other
cases, the effects may exceed the end. The sclerotic tissue may be
exuberant and form veritable tumours, designated under the name
keloids; or, obeying its retractile tendency, it will contract, compress
the neighbouring parts, interfere with their activity, and thus provoke
new disturbances.

General Reactions.—The local phenomena of which we have just
indicated the mechanism are frequently attended by general manifesta-
tions. Whenever the local inflammation is somewhat intense, numer-
ous disturbances become manifest. The temperature of the subject
rises suddenly or slowly, the appetite is lost, the tongue is coated,
digestive disorders set in, and respiration is accelerated. The patient
experiences a feeling of malaise and of lassitude; he often complains
of headache, and becomes incapable of continuing his occupation or of
fixing his attention. At times matters go still further: quiet or vio-
lent delirium occurs, the tongue becomes dry, and the lips are fuligi-
nous. The condition is disquieting, notwithstanding the fact that
the lesion has remained absolutely local.

We shall again refer to all these manifestations, which are for the
most part dependent upon intoxication. The soluble products, pro-
duced at the morbid focus, thus profoundly modify the organism and
give rise to general reactions, including fever. These reactions repre-
sent the most striking example of the relations existing between the
various parts of the economy under pathological as well as under nor-
mal conditions. We shall make a special study of this when describing
the functional synergies and morbid sympathies (Chapter XIX).

We shall now consider the mode of formation and the meaning of
the principal inflammatory processes.

Pseudo-membranous Processes

Pseudo-membranous processes are usually divided by German au-
thors into two groups. They describe under the name *croupous exu-
dation* that form which is superficial, and under the name *diphtheritic
exudations* that form which is more profound—namely, interstitial.
These expressions are bad; they lead to confusion, and must be aban-
doned. But they correspond to a just idea, or at least to a necessary

distinction. Two varieties of pseudo-membranous processes are to be admitted. In some cases it is a question of the formation of a new membrane covering up a mucous membrane, of which it reaches the most superficial parts only. In others, the pseudo-membranous appearance results from a necrosis, from a more or less profound diphtheroid gangrene. The former process is realized by certain microbes, notably by the bacillus of diphtheria; the latter characterizes the destructive affections of toxic or microbic origin. Caustics, like nitrate of silver, and the most varied microbes may produce lesions of membranous appearance. Such is the case in stomatitis, known as ulcero-membranous stomatitis, which were better called superficial gangrene of the mouth; such is also the case in muco-membranous enteritis. In these two affections the so-called false membranes are nothing else than parts or shreds of the altered mucous membrane.

There is, then, a capital difference between the two processes. The first is dependent upon a general reaction of the organism; the second is the work of a pathogenic agent. The former is characterized by the development of a concrete exudation at the surface of the mucous membrane; the latter by the exfoliation and expulsion of a pre-existing necrosed part.

Leaving aside the history of diphtheroid gangrenes, to which we shall hereafter refer, let us consider only the true pseudo-membranous process.

In the habitual conditions of life this process may be considered as always dependent upon a microbic infection. However, a specific diphtherogenic microbe does not exist. The false membrane represents a quite common reaction, which may be called forth by a great number of bacteria. It suffices to consider what occurs in the throat. Pseudo-membranous sore throats may be produced by numerous microbes. Along with Loeffler's diphtheritic bacillus, which holds the first place, are to be ranked streptococcus, pneumococcus, pneumobacillus, tetragenes, etc.

On the other hand, an agent capable of giving rise to the formation of a false membrane may in other cases produce an edematous exudation or a purulent focus: witness streptococcus or pneumococcus. The latter microbe produces false membranes, exudations very rich in fibrine, or true suppurations. The difference depends upon the virulence of the microbe, upon the seat of the lesion, and upon the condition of the subject. Secondary influences intervene in all cases, even in the case of Loeffler's bacillus. The diphtherogenic action of this microbe is manifested only on parts in contact with air; subcutaneous inoculations produce only œdema rich in fibrine, but no false membranes.

It is a law well established to-day that the morphological elements do not act except by their secretions. This law may be applied to the pseudo-membranous processes. It has for a long time been believed that false membranes were not produced except under the influence of living bacteria acting upon an altered mucous membrane. At present it is demonstrated, at least as regards the diphtheritic bacillus (the only microbe that has been studied from this point of view), that the false membrane is due to the action of toxines. It has been possible to reproduce laryngitis, bronchitis, conjunctivitis, and vulvitis, all pseudo-membranous, by simply depositing the pure toxine of the diphtheria bacillus upon the mucous membrane; but as this had already been established with regard to suppurations, the more slowly the poison is applied the greater will be the success.

It is probable that the microbic toxine acts by primarily altering the cells with which it comes in contact; but this action is slow. If vibratile cells of the trachea are taken and placed in toxine and in simple bouillon for comparison, their movements are seen to persist in both cases for almost the same length of time.

The altered cells secondarily provoke a vaso-dilatation, and then a diapedesis of leucocytes. Thus far the phenomena have nothing special. Subsequently, within twenty-four to forty-eight hours, the false membrane develops.

To explain the production of the latter, several theories have been advanced. The simplest idea is to assume an exudation of a fibrinogenic substance which coagulates on contact with the air. Wagner sustains the view that false membranes are produced by the cells of the tissue, which unite by means of prolongations.

To-day the consensus of opinion is that exudation is constituted, on the one hand, of fibrinogenic substance, and, on the other, of altered cells. The fibrinogenic substance escapes from the vessels, and finds itself in the best conditions for coagulating; it is in contact with the air, it meets with dead leucocytes, which here, as everywhere else, play a great part in coagulation; it is spread out upon a mucous membrane whose cells are diseased. Now it is known, from Cohnheim and Weigert, that the epithelial as well as the endothelial cells do not oppose coagulation of exudations except when they are intact. Finally, a certain rôle is to be attributed to the cells of tissues, which become fibrinified according to the process described by Weigert under the name of coagulation necrosis.

Thus made up at the expense of the fibrine of blood and of the cells, false membranes present quite variable aspects. They may be seen in serous exudations, where they float in the liquid; elsewhere more abundant, they line the two surfaces of the serous membrane and

may bring them to adhesion. Finally, they frequently have their seat upon the surface of a mucous membrane, to which they adhere more or less intimately.

Should one of these false membranes be stripped off, the ulcerated surface becomes exposed, slightly bleeding; and this proves that we are in the presence not of a simple deposit, but of a profounder process.

The detached false membrane is quite resistant; it does not disintegrate when agitated in the water, thus being distinguished from pultaceous layers or mucous concretions. It is dissolved by lime water and by hypochlorite of soda; its richness in fibrine explains why it decomposes oxygenated water.

Examined microscopically, it is found to be composed of anastomosed fibrinous threads, sending out prolongations which attach themselves to the subendothelial tissues by a series of arcades; this explains why the production is adherent. The fibrine appears under the form of lamellæ, compact masses, or spiral threads. In the midst of the fibrine are seen fat, mucine, degenerated cells, and, in most cases, numerous microbes.

Thus constituted, the false membrane may grow by the addition of new layers of fibrine and be reproduced when it is stripped off. The considerable quantity of fibrine which may thus be eliminated is not to be wondered at. Dr. Dastre has shown that this substance is very rapidly produced in the organism. If the greater part of the blood of a dog be defibrinated and again introduced into the vessels, it will soon be found that the blood is as rich in fibrine as normally.

When a false membrane occupies the surface of a mucous membrane—that of the throat, for example—a moment will arrive in fortunate cases when the secretions of the subjacent glands will detach the pathological productions and bring about their exfoliation; the remaining adherent *débris* will be picked up by the phagocytes. This process may be assisted by means of pilocarpine, which, by favouring glandular secretion, hastens exfoliation of the false membranes. In some cases the latter disappear in consequence of a histochemical transformation; they undergo a granular or a hyaline degeneration.

In other cases, in tissues, and particularly in serous membranes, the false membrane, far from disappearing, becomes organized. The fixed cells and the wandering cells proliferate, following the false membrane, which serves them as a guide. Simultaneously the tissue becomes vascularized. In this way adhesions are formed, which may subsequently be absorbed, undergo sclerotic transformation, or become infiltrated with calcareous salts.

The production of false membranes is to be considered as a responsive process of defence. It is a barrier opposed to the penetration

of microbes or of toxines. In some cases it is a re-enforcement of tissues, which prevents their destruction under the influence of pathological causes. The false membranes developed upon serous membranes are intended for the same end.

Reactions often exceed the end, or, after having been useful, become harmful. The diphtheritic false membrane may by its seat produce grave and fatal mechanical disturbances. The adhesions of serous membranes embarrass the movements of subjacent viscera, cause deformities, compress important organs or excretory passages, and thus give rise to a whole series of new morbid manifestations.

SUPPURATION

Suppuration is one of the terminations of inflammation. It is characterized by the production of a liquid exudation, containing numerous necrosed cells, designated by the name pyocytes or pus cells.

Characters of Pus.—According to the microscopical aspect, three varieties of pus are usually admitted:

Phlegmonous pus, the laudable pus of the old authors, is a yellowish-white, creamy, thick, odourless liquid. It is met with in phlegmons and in purulent pleurisies.

Caseous pus is more consistent. It resembles certain soft cheeses; hence the name given to it.

Lastly, *thin pus* is formed of a serous liquid floating upon clots and frequently containing necrosed or sphacelated elements and fatty acids; it often exhales a disagreeable or fetid odour.

The *colour* of pus is no less variable. Usually yellowish, it may be of orange, brownish-red, or greenish colour. As to blue pus, the expression is bad; there is no suppuration presenting this colour. Under this name have been designated cases where dressing materials have imbibed a colouring matter—pyocyanine of Fordos—produced by a special bacillus (*Bacillus pyocyaneus*) which is not pyogenic by itself.

No relationship exists between the aspect or the colour of pus and the cause which has determined its development. We shall make an exception only of the suppuration of pneumococcic origin, which is thick, greenish, and rich in fibrine, often having the aspect of false membranes. It is rather owing to the points where it is developed that suppuration presents particular characters. In subcutaneous or pleural collections the pus is phlegmonous, thick; in the meningeal membranes of the brain it is greenish; in the liver, of chocolate colour; and reddish in the lung. When it is of osseous origin it often contains fat and small splinters of bone. If it takes origin in the glands of the skin it produces a furuncle or a carbuncle—a lesion remark-

able for the presence of sphacelated fragments of cellular tissue, which constitute the core.

There may also be found in pus foreign bodies, tissue fragments, elastic fibres, animal or vegetable parasites, hydatids, actinomycetes, organic liquids, bile, milk, urine, fæcal matters, and alimentary fragments. These various substances are of great importance from a semeiological standpoint; they inform us as to the origin of pus and as to the possibility of organic fistulæ.

It is generally easy to recognise pus. In case there should be any difficulty, for example, in the presence of inspissated mucus or of steatomatous contents of certain sebaceous cysts, it suffices to make a microscopical examination. The same method of exploration is useful in determining the presence of pus in certain organic liquids. In the urine, for example, it may be recognised by the addition of ammonia, which causes a curdled precipitate. In certain cases, to which we shall again refer, serous membranes contain chyliform exudations, which are formed of an emulsion of fatty matter. It is easy to recognise the nature of the latter. The microscope reveals the absence of pus cells, and ether completes the demonstration by dissolving the fat. Ether may also aid in the recognition of certain collections rich in cholesterine; it dissolves this substance, and, on evaporation, leaves a deposit of crystalline lamellæ the shining aspect of which is very characteristic.

Histology of Pus.—Microscopic examination, which is to be resorted to in doubtful cases, shows in pus a great number of cells known under the generic name pyocytes (pus cells). According to their aspect and origin, they are divided into two groups:

A. Large cells—namely (1) leucocytes, of which three varieties are admitted: mononuclear, polynuclear, and eosinophilic leucocytes; (2) Glüge's corpuscles, made up of the union in spherical masses of fatty granules arising from the destruction of cells; and (3) spheral cells derived from connective tissue.

B. Small cells, including (1) small white globules, called lymphocytes; (2) round cells derived from connective tissue; and (3) perhaps free nuclei.

Chemical Constitution of Pus.—Chemically, pus is a neutral liquid, sometimes alkaline, exceptionally acid. Its density varies from 1,020 to 1,040. Allowed to stand, it does not coagulate, but separates into two layers: a superficial layer, the pus serum, and a profound layer, containing cells. In general, there are 700 or 800 parts of serum to 200 or 300 parts of globules, but these figures are very variable. In some instances pus contains only 25 per 1,000 of morphological elements.

Pus includes various albuminoid matters—serum, globuline, nucleo-albumin, albumose or peptone, fat, lecithine, and, in old foci, cholesterine. It also contains glycogen, which is contained in its cells; ptomaines, ferments possessing the property of peptonizing gelatine; and pigments derived probably from the colouring matters of blood and of tissues. It contains no urea and no sugar, except perhaps in cases of diabetes.

Mechanism of Suppuration.—The origin of the liquid constituting the pus serum is evidently to be traced to the blood serum. That exudation depends upon a process of osmosis is inadmissible. In fact, in this hypothesis it would invariably have the same chemical constitution and contain the same elements as the blood plasma and in the same proportions. The differences observed from one case to another indicate that we have to deal with a true secretion: the altered cells draw certain substances in an elective manner; the vascular endothelia, disturbed in their function by the pathogenic cause which provokes suppuration, now allow one substance, now another, to pass.

When the exudation is formed, its composition is subject to modification by neighbouring cells or those which enter into it, and by pathogenic agents, particularly by the microbes which multiply in it. This is why albumoses and peptones are almost constantly present. These bodies, which are not found in the blood, have a local origin as the result of the action exercised by cells or microbes upon albuminoid matters. At any rate, it is useless to dwell upon these facts, as we have already studied an analogous question in presenting the general history of inflammatory exudations.

The cells that are found in pus are derived from two sources. The smallest number originate locally; the cells of connective tissue, the adipose cells, perhaps even some differentiated cells, are transformed into round elements. But the majority of purulent cells are of hemic origin. These are leucocytes, which, having collected in great numbers, escape from the vessels by diapedesis and accumulate at the point attacked. Some of these cells remain living; the majority succumb in the struggle they sustain against the pathogenic agent—i. e., the cause of inflammation. It is precisely this death of the cells that characterizes suppuration. Hence the exudation comprises innumerable cellular elements, which, no longer of any use, represent nothing more than true foreign bodies, which are to be reabsorbed or eliminated. It is under these circumstances that the physician frequently intervenes, and, by an incision, permits the escape of the purulent collection. In many instances such collections are again formed, often with extraordinary rapidity: within forty-eight hours a pleuritic exudation of one or several litres may be reproduced. Now, if we

remember the number of leucocytes present in such an exudation, we can not but be astonished at so great a multitude of cells which the blood can furnish.

Under normal circumstances the blood contains 6,000 leucocytes to the cubic millimetre, which, for the 5 litres contained in the human body, amounts to 30,000,000,000. Pus, having on an average 125,000 white blood corpuscles to the cubic millimetre, contains 125,000,000,000 to the litre, and that means that it contains four times more than the blood mass.

We are thus led to ask, Whence come the innumerable leucocytes which are found in the exudation? Their presence seems to be accounted for by a previous leucocytosis. Instead of the normal figure of 6,000, the blood contains 15,000 to 20,000, and even 36,000 leucocytes per cubic millimetre. These leucocytes are produced in the hematopoietic organs—in the spleen, which is often increased in volume; in the lymphatic glands, which are swollen; and, above all, in the marrow of the bones. The osteomedullary tissue, overcharged with fat in a state of rest, is modified as soon as the organism is in need of leucocytes. The pathogenic agent, which locally determines an inflammation tending to become suppurative, directly or indirectly stimulates the vitality of the marrow of bones; the fat is absorbed, the cells are multiplied and fill up all the tissue. These modifications, so marked under a histological examination, are already appreciable to the naked eye: the marrow assumes a red colour, recalling the aspect which it presents at birth, where it is very rich in cells. This is a return to the fœtal condition.

The microscopic examination of pus, by showing the pathogenic agent, also informs as to the cause which has given rise to the process. In the majority of instances the development of suppuration is dependent upon the presence of microbes which may be brought to light by simple microscopic preparations. In order to obtain precise information, however, it is indispensable to have recourse to bacteriological cultures.

Pyogenic Agents.—It has thus been recognised that suppuration may be caused by very numerous microscopic agents, which we shall divide into five groups:

1. *Bacteria habitually Pyogenic.*—They are normally encountered upon our integuments, and, although they may give rise to very varied manifestations, they especially provoke suppuration. These are *Staphylococcus aureus* and *albus*, streptococcus, pneumococcus, colon bacillus, and *Micrococcus tetragenes*.

2. *Specific Pyogenic Bacteria.*—They produce suppurations which, from a clinical standpoint, present a particular evolution. Only three

microbes enter into this group: gonococcus, the bacillus of soft chan-
cre, and the bacillus of glanders.

3. *Bacteria accidentally Pyogenic.*—This group comprises quite
numerous species, which produce more or less well-differentiated le-
sions, and may in certain cases cause suppuration. These are, for
example, the tubercle bacillus, which causes most of the cold abscesses,
and the typhoid .bacillus, which may also produce pus, notably in
bones.

4. *Vegetables capable of becoming Pyogenic.*—Here it is a question
of parasites more elevated than bacteria. Such are streptothrix (of
which *Streptothrix bovis* or actinomycetes is the most important), as-
pergillus, and oidium.

5. Finally, the last group comprises the *animal pyogenic parasites*
—namely, the sporozoa capable of inducing suppuration. The most
important is the amœba of dysentery, which, it seems, may cause
abscesses in the liver.

Of all these pathogenic agents, staphylococci and streptococci are
most frequently encountered. In bringing together a certain number
of well-prepared statistics, it is found that, out of 144 cases, staphylo-
coccus has been discovered 114 times and streptococcus 26. Fre-
quently, several species are met with united in the same focus: staphy-
lococcus and streptococcus often coexist; they may further be asso-
ciated with pneumococcus and with colon bacillus. Such polymicrobic
foci are generally transitory, for one species gradually attains the
upper hand, commonly staphylococcus, and the others disappear.

When a pyogenic species is introduced into an organism suppura-
tion develops, especially if the bacteria are numerous. We have already
cited figures given by different authors. W. Cheyne finds that 250,-
000,000 cocci must be injected in order to produce an abscess. Bujwid
declares that 1,000,000,000 is insufficient. The differences are ex-
plained by the variability of virulence. In order that suppuration may
appear, microbes of a medium activity are required. If too attenuated,
they are destroyed without having produced any disturbance; if too
energetic, they at once invade the economy and provoke a general in-
fection, as septicæmia; in both cases the local lesion is wanting. The
effects also vary according to the point where microbes are intro-
duced. In cartilages suppuration is very rare. What is more curious
is the fact that tissues whose structure is nearly identical behave very
differently: abscesses are frequent in the brain but exceptional in the
spinal cord. Among the muscles, only three are generally affected:
the deltoid, the sterno-cleido-mastoid, and the iliac psoas. The lung
does not easily suppurate, at least the healthy lung; but when it is
already altered, pus cocci develop in it with the greatest facility. The

digestive canal is often traversed by the same cocci, which, if the mucous membrane is intact, are able to develop and produce no accident whatever.

The most sensitive part of the organism is the anterior chamber of the eye; it is 8,600 times less resistant than the subcutaneous cellular tissue. As regards the serous membranes, the variations are quite considerable: the arachnoid and the pleura easily suppurate; the peritoneum is endowed with a very powerful antimicrobic action.

The pyogenic agents may be directly introduced into our tissues— for example, by an instrument charged with microbes. But in connection with mechanical agents there is a fact of considerable importance on which we have already dwelt. A clean-cut wound, even when it is contaminated, often unites by first intention. This is true of nearly all wounds, even of operative wounds which appear the most perfect. Ideal asepsis, therefore, is an illusion. Numerous pyogenic microbes which produce no disturbance are found under the best dressings. If, on the contrary, the wound is contused, or the borders lacerated, or the tissues mangled, the microbes develop with the greatest facility.

Suppuration is also favoured by the presence of a foreign body. For example, the extraction of such a body often suffices to arrest the discharge without any other intervention.

Chemical agents exert upon the tissues an analogous action, which therapeutists have turned to account: Thus, Croton oil, when spread upon the surface of the integuments, gives rise to the formation of pustules. Antiseptic substances, if too concentrated, favour suppuration. Before killing the microbe they cause death of the cells, and consequently diminish the resistance of the organism; they produce an effect which is just the reverse of the one expected.

In cases where suppuration seems to appear spontaneously—namely, without traumatism or direct inoculation—it is often dependent upon a modification in the normal secretions, which, being diminished, are no longer capable of sweeping the excretory passages. The bacteria enter them and develop. Their action is often favoured by the presence of some foreign body obstructing the canal. Thus, a hepatic calculus, by plugging the bile duct, permits the colon bacillus to invade the biliary channels and induce a suppurative angiocholitis. Likewise, if the cavity of the ileocæcal appendix becomes obstructed, the microbes contained in it will be apt to exercise a pyogenic rôle. This appendicitis may be experimentally produced in the rabbit. Ligation of the appendix is sufficient to transform it into a purulent pouch. But if a cutaneous fistula be formed at the same time the ligature is applied, thus permitting the escape of the liquid produced within the intes-

tine, no suppuration will appear, no matter how small this opening may be.

In the course of infectious diseases the secretions are often diminished or suppressed. In typhoid fever, for example, the mouth is dry. Formerly, when no antiseptic precautions were taken, the bacteria of the buccal cavity entered Steno's duct and quite often caused parotiditis. As is known, this event has at present become altogether exceptional.

Finally, the pus cocci manifest a great tendency to invade parts already diseased. Lesions of the skin and mucous membranes and pulmonary alterations easily become the seat of suppuration. Various poisons probably favour the development of suppuration by altering the tissues through which they are eliminated. The pustules of acne and the furuncles observed in cases of iodism and bromism may be explained in this manner. It is perhaps convenient to admit a more complex process. These substances cause digestive disturbances ending in an exaggeration of gastrointestinal putrefactions. Now, it is demonstrated that substances thus taking their origin may cause furunculosis (Bouchard). This form of cutaneous infection is easily cured by the administration of certain insoluble antiseptics—benzonaphthol or beta-naphthol; the fermentations decrease, and the cutaneous glands, no longer having to eliminate an excess of toxines, become capable of resisting microbic invasion.

Likewise, diabetes favours suppuration in consequence of humoral modifications. Clinics abound in illustrations, and experimental pathology furnishes similar results. A number of staphylococci, which produce nothing when injected beneath the skin, cause an abscess if a cubic centimetre of a 25-per-cent solution of glucose be introduced with the microbe. They cause a phlegmon if the sugar is injected into the veins.

Lastly, all causes which weaken the organism favour suppuration. It is well known how frequently abscesses occur during convalescence from grave diseases.

The suppurative focus, of which we have just studied the constitution and mode of development, may remain local or give rise to secondary foci. In order for the microbic process to become generalized, the pathogenic germs must of necessity invade the circulatory system. In certain cases their passage into the blood is preceded by the development of a phlebitis. The microbe alters the walls of a vein, and the blood coagulates there. The clot invaded by the pathogenic agents subsequently breaks down, and its *débris*, serving as vehicles for the microbes, gives rise to suppurative lesions at different points. In other instances the pus cocci reach the blood either by passing through the

venous walls without occasioning previous coagulation, or after having penetrated the lymphatics and traversed the glands, which have been able to retain them for an instant.

Once in the blood, the microbes do not remain there, as this medium is unfavourable for them. They therefore deposit themselves in the various tissues. From that moment three results are possible: The microbes may be destroyed by phagocytes; they may be at least partially eliminated by the sweat and the urine; or they may multiply and produce visceral abscesses according to a procedure identical to that which explains the formation of the primary abscess.

When a focus is developed, whether primary or secondary, subcutaneous or visceral, the organism tries to react: it forms a barrier which tends to circumscribe the infection. In fortunate cases the microbes diminish and in the end disappear, so that the focus passes through five successive phases: It at first contains living and virulent microbes; then living, but attenuated ones; then cadavers of microbes which are still visible under the microscope, but which can no longer be cultivated; at last it no longer contains any bacteria, but it is sterile.

The nonmicrobic suppurations are frequently observed in old lesions, provided there be no communication with the exterior. They are often met with in the Fallopian tubes; in the liver, in which about forty observations have been collected; and more rarely in the brain and around the kidney.

Generally well borne, these foci may, however, give rise to various accidents, despite the absence of living microbes, notably to paroxysms of fever, but once opened up they heal with the greatest facility.

In view of the fact that purulent collections may in time become sterile, we may inquire whether in certain cases pus could not develop under the influence of simple chemical substances without the intervention of any living element whatever. This question, which has given rise to most animated controversies, is to-day solved. Numerous experiments made in animals and therapeutic inoculations practised in man have established that pyogenic properties may be attributed to a great number of substances, of which we shall mention metallic mercury, calomel, silver nitrate, turpentine, Croton oil, antipyrine, solvines, sapotoxine, digitoxine, etc. The chances for suppuration to be effected will be the greater the larger the quantity of substances injected, the more concentrated the solutions used, and the more slowly they are introduced. Five drops of turpentine injected at once does not produce any pus; the same quantity introduced from a small celluloid pouch, from which it should flow slowly, will give rise to its appearance. The latter experiment, which we owe to Poliakoff, undoubtedly

explains a great many discordant results. Other contradictions are due to the fact that effects vary according to the animal species. Non-microbic suppuration is produced in the rabbit with much more difficulty than in the dog. Thus it is seen that generalization of particular cases has, as always, led to error.

When it is remembered that the microbes themselves act only through the agency of the soluble matters which they produce, it is not astonishing that certain chemical compounds should have a pyogenic action. The cultures of *Staphylococcus aureus* contain an alkaloidal substance, Leber's phlogosine, which is probably nothing else than a product of the true toxine, an albuminoid matter, isolated by Christmas, the injection of which causes suppuration.

Similar results have been obtained with the cultures of streptococcus, with the extracts of putrid meats, and with ptomaines like cadaverine. Behring has demonstrated that the pyogenic power of the soluble products is annihilated by iodoform. Thus is explained the action of this drug, which, although feebly antiseptic, exercises such a favourable influence upon suppuration.

Finally, from the important researches of Buchner, it appears that the protoplasm of bacteria contains pyogenic substances. It may be concluded from this fact that when microbes are destroyed and disintegrated the pyogenic substance contained in them is given off, spreads in the focus, and may favour its extension.

To sum up, suppuration is a common process which may be due to a great number of chemical substances and animate agents. Clinically, pus is almost always produced by microbes. But the latter act only through the agency of the soluble products which they secrete or through the substances contained in their protoplasm. We must therefore conclude that suppuration is always occasioned by chemical substances.

Evolution of Purulent Foci.—Once formed, the purulent collection tends to make its way in the organism. It advances and extends by means of the ferments which the pus contains and which digest the tissues. It thus directs itself toward the exterior or toward a hollow organ, preferably following the paths half traced by the aponeurotic or muscular interstices, and the vascular or nervous sheaths. Then the collection opens and the pus flows out.

At the same time a work of reparation begins, which in abscesses experimentally caused is already appreciable on the second day. Buds are formed, which tend to fill up the suppurating cavity; they contain voluminous cells, destined to free the focus from the cellular cadavers that may be found there. The buds that come in contact unite and give origin to a soft or hardened cicatrix, which is some-

times exuberant. In the latter case it constitutes a sort of tumour called keloid.

In certain cases pus becomes encysted, and may undergo fatty degeneration and assume the aspect of chyle.

Chyliform collections have chiefly been observed in serous membranes. They have been the subject of numerous discussions. In certain cases there has been, it seems, a true collection of chyle, due to rupture of an important vessel or even of the thoracic duct. In most cases it is a primarily purulent collection whose microbes have succumbed, and whose cells, having undergone granulo-fatty degeneration, have completely disintegrated; the freed fat has been emulsified and has imparted to the liquid a milky aspect. Such collections are mainly observed in the pleura, peritoneum, and tunica vaginalis.

If the liquid part is absorbed, there remain thick, caseous masses, which may become infiltrated with calcareous salts.

Symptoms.—The development of a purulent focus is expressed by a series of symptoms, the principal ones being the four so-called cardinal symptoms, namely, pain, heat, redness, and swelling.

Pain is generally the first phenomenon by date. It is due to an increased flow of blood and to active congestion occasioned by the introduction of a pyogenic agent. The arrival of arterial blood is expressed by a slight hyperæsthesia of the skin and by a sensation of throbbing synchronous with the pulse. At the end of a certain time the pulsatile pain gives place to a sensation of constriction, due to distention of the resisting parts and to stretching of the nervous terminations. Subsequently, when the purulent collection is produced, the spontaneous pain disappears, and profound pain is caused only on pressure.

Shortly after the beginning of the painful manifestations, sometimes at the same time, more rarely before, *pain* and *redness* appear. These two phenomena are less constant; they are wanting when the focus is profound—for example, when it is inclosed in the cavity of a bone. Therefore, particularly appreciable in cases of superficial lesions, they are related to the increased circulation of blood and to karyokinesis. However, even in cases of profound suppurations, the temperature may rise in those regions of the skin which cover the parts attacked. Local thermometry reveals a rise of temperature by a few tenths of a degree.

The fourth phenomenon, *swelling,* is evidently appreciable only in cases of foci superficially situated or tending to bulge outward. However, even if the collection is profound, one may often observe a sometimes considerable œdema in the integuments which cover it. The semeiological importance of this phenomenon is very great. In

cases of pleurisy, for instance, the œdema of the thoracic wall indicates almost surely the purulent nature of the exudation; similarly, in cases of suppurative osteomyelitis, the integuments are frequently infiltrated with an abundant serous exudate.

Besides the four cardinal phenomena above indicated, there are functional disturbances to be considered. The glands in the neighbourhood of the focus may secrete in exaggerated amounts or give origin to liquids of an anomalous constitution; in other cases, on the contrary, the secretion stops.

The muscles often lose their power. Stokes has made known the paralysis of the diaphragm occasioned by purulent exudations of the diaphragmatic pleura. The palate is equally impotent in cases of intense phlegmonous angina. Finally, in peritonitis, tympanites is likewise explained by a paralysis of the nonstriated muscular fibres of the intestine.

The natural tendency of purulent collections is to make their way outward and be evacuated. Once open, the course is toward a cure; but a favourable evolution may be hindered by manifold causes. The opening may be insufficient; then the pus tends to propagate toward other regions and causes channels and cavities; or the fistula will now and then close up, with the result that various accidents will occur, due to the retention of the pus; or the opening will be made into an important organ and be followed by grave or fatal accidents; or, finally, the focus will be secondarily invaded by germs, which will induce putrid fermentations.

When the evolution seems to be on the point of terminating, an accidental cause may revive the process. Transitory indisposition, indigestion, fatigue, nervous shock, moral impression, sometimes untimely intervention, will determine the spread of the suppuration.

From the standpoint of their course, abscesses are often divided into two groups: hot abscesses and *cold abscesses.*

Hot abscesses include *circumscribed phlegmon* and *diffused phlegmon.*

Circumscribed phlegmon is a collected, well-defined suppuration, generally surrounded by a membrane called *pyogenic.* Diffused phlegmon, badly limited, tends to extend and invade the neighbouring parts; it is accompanied by grave phenomena, and in some respects it resembles erysipelas; at any rate, it is streptococcus which intervenes in both cases.

Cold abscesses are at present often considered as tuberculous abscesses. It is quite certain that tuberculosis is the principal cause of the suppurations which are designated as "cold," because they arouse no local or general reaction. But the same process may be

referable to very numerous agents. The *Staphylococcus aureus* may produce, especially in the skin, chronic abscesses, the evolution of which in every way recalls that of a tuberculous focus. These abscesses are mainly observed in children: their nature has been demonstrated, on the one hand, by cultures which have revealed the presence of the staphylococcus, and, on the other hand, by direct inoculation of the virulent products into guinea pigs—inoculation that has not been followed by the development of tuberculous lesions.

Staphylococcus has exceptionally been able to produce analogous lesions. The typhoid bacillus especially locates itself in the marrow of bones in convalescents from typhoid fever, and causes chronic osteomyelitis, which, without the assistance of bacteriology, one would be tempted to consider tubercular.

There exists a last variety of nontuberculous cold abscesses: these are produced by actinomycetes. It has exactly the same course as in tuberculosis. Error will be avoided by a careful examination of the pus. There will be found in it small yellow grains, which have been rightly compared to the flower of sulphur. Examined under the microscope, these small masses appear to be formed of radiated filaments terminating by clublike swellings at their periphery.

GANGRENE

Definition.—Gangrene is a morbid process essentially characterized by the mortification and putrefaction of tissues.

Mortification does not suffice to define the process. If it exists alone, the condition is designated as necrobiosis. In order that gangrene may occur there must be putrefaction in addition to necrobiosis. Now there can be no putrefaction without microbes. Therefore gangrene is always of microbic origin, while necrobiosis may be produced by most varied agents.

Let us suppose, for example, that the principal artery of one of the lower extremities is obliterated and the circulation interrupted: gangrene will appear, for the microbes of the integuments will invade the parts deprived of circulation. Without the intervention of microbes there would be only a simple necrobiosis. In fact, if the obliterated artery be that of a part inaccessible to air—one of the cerebral arteries, for example—the tissue will degenerate; in this particular case there will be softening, but, owing to the absence of microbes, no gangrene.

The microbes causing gangrene act upon the altered tissues as they would upon the tissues of cadavers. Between gangrene and cadaveric putrefaction, however, there are decided differences. First, the affected parts are still the seat of certain reactions. There is an influx of

serum, lymph, and blood pigment; the bacteria, attacking the exudate, produce new fermentations therein. On the other hand, whatever may be the extent of the lesions which give origin to the gangrene, it is inadmissible to assume that all the cells are attacked. Some of them survive, at least those that are in the peritoneum, and these are able to react and thus impart a special character to the process.

We shall state, therefore, that cadaveric putrefaction is a fermentation in dead tissues. Gangrene is a putrefactive fermentation in tissues altered but not completely deprived of life.

Efficient and Accessory Causes.—There is no gangrene microbe. A great number of bacteria may give rise to this process.

Pathogenic agents have been divided by some authors into two groups: those capable of inducing gangrene in healthy tissues—namely, the two successive stages of necrobiosis and of putrefaction—and those which require the pre-existence of necrobiosis and which are simply putrefactive.

This division, which possesses a certain importance, is not perfect, for, even in the case of the most active agents, accessory or predisposing causes play a considerable part. It is altogether exceptional to see healthy tissues invaded by gangrene.

The causes favouring the development of gangrene may be divided into two groups, according as they act directly on the tissue to lessen its vitality, or indirectly, by means of the vessels, the nervous system, or the blood. Each group comprises a certain number of secondary causes, which may be classified in the following manner:

Agents.

Direct alterations of tissues by ....
- Mechanical.
- Physical.
- Chemical.
- Animate.

Indirect alterations by
- Circulatory disturbances.
  - Vascular compressions and obliterations.
  - Arteritis.
  - Œdema.
- Nervous disturbances.
  - Encephalo-myelitic alterations.
  - Neuritis.
  - Raynaud's disease.
- Dystrophic disturbances.
  - Humoral alterations.
  - Auto-intoxications.
  - Exogenous intoxications.
  - Infections.

The influence of alterations produced by various traumatic agents is evident. Ragged, contused wounds, mechanical compressions and lesions of vessels and nerves, and comminuted fractures considerably favour the development of all microbes in general, and of those of gangrene in particular.

Intense heat and cold act in the same way by diminishing the resistance of the cells and disturbing the circulation. Chemical agents are still more important. Caustics, venoms, organic liquids, and bile or urine abolish the resistance of the tissues in which they spread. Urinary infiltration, consecutive to rupture of the urethra, for example, greatly predisposes to suppuration and gangrene. The intervention of animate agents which prepare the way for the action of gangrenous agents is much more complex, and seems to be concerned not in a local lesion, but in a disturbance of the entire organism.

At the head of causes acting indirectly we shall first of all cite those which disturb the blood circulation, notably those diminishing the supply of arterial blood. Whether arteriosclerosis, acute arteritis, thrombosis, or embolism be present, gangrene can not appear without the intervention of microbes. This is demonstrated by the classical experiment of Chauveau on twisting the testicle. This operation entails a simple atrophy of the testicle; but if before practising it microbes be injected into the veins, the organ deprived of its vessels will become an easy prey and will be attacked by gangrene.

The arterial obliteration does not need to be complete. A simple stricture suffices, especially when connected with an infectious process. The microbes located in the vessel walls secrete substances which complete the annihilation of the resistance of the surrounding tissues. Vascular spasm may have the same effect. In symmetrical gangrene of the extremities, or Raynaud's disease, simply a vaso-constriction is produced, followed by small patches of gangrene, which are to be attributed to the microbes of the skin.

Disturbances of the venous system are much less important, because either the re-establishment of the circulation is easier or the accumulation of dark blood is less harmful to the tissues than the absence of arterial blood. Œdemas, for example, even when abundant, are rarely invaded by gangrene; phlebites are almost never followed by this accident.

The influence of the nervous system is evidenced by numerous facts; the eschar, which rapidly ensues in hemiplegic or paraplegic patients, is explained by the nutritive disorders which permit microbic invasion. Lesion of a nerve may have the same effect. Brown-Séquard has shown that section of the sciatic nerve in the guinea pig is followed by gangrenous phenomena in the extremities. Here it is a matter of secondary infection, which is avoided by protecting the paw against the action of the external germs. The inoculation of streptococcus beneath the skin of the ear of a rabbit no longer produces a simple erysipelas, but a gangrenous inflammation, provided the auriculo-cervical nerve, which furnishes sensibility to the region, be sev-

ered at the same time. In man, confirmation of these facts is found in those cases in which peripheral neurites produce sphacelus and at times massive gangrene.

Finally, modifications in the composition of the blood play a considerable predisposing part. It suffices to mention the influence of diabetes and the frequency of gangrene in this affection. In other cases it may be a poison—ergot or mercury, for example—which, by modifying the circulation or the vitality of the cells, permits the development of the gangrene germs.

As to infections, their influence is complex. They act by disturbing the circulation, paralyzing the nervous system, causing auto-intoxication, altering the various protective organs, diminishing the secretions, and by disturbing nutrition. Gangrene results from the synergic action of these various factors.

Bacteriology of Gangrene.—The microbes capable of producing gangrene are divided into two groups. There are, first, those which especially possess this power. The chief representative is a bacillus described by Pasteur under the name septic vibrion, also known to the school of Lyons as bacillus of gangrenous septicæmia, and by the German authors as bacillus of malignant œdema, but better termed bacillus of gaseous gangrene (page 111).

The disturbances caused by this bacillus in man have been variously designated as malignant œdema (Pirogoff), acute purulent œdema, swift gangrene (*gangrène foudroyante*, Maisonneuve), invading traumatic gangrene (Bottini), and as gangrenous septicæmia (Chauveau). These various expressions can not be accepted, since they give rise to confusion. The terms gangrenous septicæmia, and that of septic vibrion, applied to the microbe, have only served to lead to numerous errors. It is therefore better to adopt the expression gaseous gangrene, which has the advantage of recalling the nature of the phenomena observed.

As is known, the microbe of gaseous gangrene is an anaërobic bacillus. It is very widely distributed, and is found abundantly in the soil, on vegetables, and in the mud of waters; it is encountered almost constantly in the residue upon porcelain filters.

Poincaré and Macé have found it in alimentary preserves, vegetable or animal.

This ubiquity explains its presence in the bodies of living beings. It may be found in the saliva, and it is often met with in the intestine, especially in the horse. Discharged with the fæcal matters, it is spread in abundance upon the soil.

Being anaërobic, the bacillus can not develop on solution of continuity exposed to the air; it can only vegetate in ragged ones and in

contused tissues. The recent investigations of Penzo and of Besson have even established that the spores of this bacillus, freed from toxine, do not produce any disorder; they do not act except when another microbe is injected with them, or when profound lesions are produced in the tissue. Thus, that which occurs under natural conditions where the gangrenous bacillus is introduced into wounds along with foreign bodies, earth, and numerous microbic germs, can be experimentally produced.

There exist other microbes that may behave like the bacillus of gaseous gangrene, but they have mainly an experimental interest. A few of them, however, have been encountered in man, but in an exceptional manner.

The second group which we must study is represented by a series of bacteria which are gangrenous only on occasion. These are the pyogenic microbes, notably *streptococcus, staphylococcus* and *proteus*. We have shown that these agents begin by exciting necrosis at the point of their introduction. If, however, the organ is vigorous, reaction appears and is expressed by suppuration. On the other hand, if the organ is weakened, altered, or incapable of sufficient reaction, necrosis attains the upper hand and gangrene develops. Reciprocally, the bacteria which produce gangrene, like the bacillus of gaseous gangrene, only cause abscesses in resisting animals. There are, then, numerous transitions between suppuration and gangrene; the existence of gangrenous phlegmons is the clinical proof thereof. The experimental proof is furnished by a well-known experiment of Bujwid: Staphylococcus, the pyogenic agent *par excellence*, causes gangrene when sugar is conjointly introduced into the organism.

Localization of Gangrenous Process.—All parts of the body may be attacked by gangrene, provided they communicate directly or indirectly with the exterior.

The *skin* is often attacked; the most diverse lesions, such as erysipelas, impetigo, herpes zoster, the pustules of smallpox and varicella, at times even simple abrasions, may be followed by gangrenous patches. But in order that this eventuality may be realized, a special debilitation is required in the subject, whether he be a convalescent or suffering with a chronic affection. Thus are developed the eschars upon the sacrum, following some minute lesion, in convalescents from grave fever, and notably from typhoid fever.

In certain cases gangrene is accounted for by the previous production of an *arteritis*, which, obliterating the principal vessel of a limb, abolishes the resistance of the parts depending upon it. Sometimes arterial alteration is due to a localization of the agent of the principal disease; oftener it depends upon a secondary infection. It

is generally streptococcus that is met with, and this microbe may be found in the condition of purity in the vascular clot and the sphacelated tissue.

In other instances it is a chronic arteritis which, by a similar mechanism, causes gangrene; by producing obstruction of a blood vessel it permits the development of the skin microbes. Such particularly is the process which explains senile gangrene. The focus comprises various bacteria, some of them common, others less common, as was the one found by Tricomi in a case of this kind.

Analogous considerations are applicable to *mucous membranes*. In the mouth the gangrene called *noma,* which is to-day extremely rare, occurs in consequence of infectious diseases, especially of measles, attacking weak and poorly kept children. The lesion is occasioned by slender bacilli (Schimmelbuch, Babes), more frequently by streptococci. It is to the same common bacteria, to ordinary pyogenic microbes, and to saprophytes that the patches of sphacelus often observed in grave diphtheria cases are to be attributed. In gangrenous parotidites Girode has found the pneumococcus associated with a slender bacillus.

The respiratory apparatus is quite frequently attacked; *necrotic laryngites* have been noted during convalescence from serious infections, measles, and typhoid fever. The lung especially deserves to be studied; it may be the seat of two orders of lesions. In a certain number of cases gangrene reaches the bronchial terminations; this is *gangrenous bronchitis*, the *curable gangrene of the bronchial terminations*. In persons suffering with chronic bronchitis, it is noticed that at a certain moment the expectoration and breath assume a characteristic odour, but the general condition remains good; the lesion is superficial, and is easily cured under the influence of eucalyptus and hyposulphite of soda. As to the microbes encountered, they are staphylococci, streptococci, pneumococci, a long, spore-bearing bacillus described by Lumnitzer, at times higher parasites, such as leptothrix, oidium, and actinomycetes.

The same microbes, although the evolution be different, are met with in *parenchymatous gangrene of the lung*. These are pneumococci, streptococci, tetragenus, leptothrix, spirilla, and agents of putrefaction. There are certain cases where bacteriological examination reveals the exclusive or predominating presence of a streptococcus or of *Staphylococcus aureus*. With the latter microbe Bonome has been able to reproduce in the rabbit gangrenous foci, which he quite rightly compares to anthrax of the lung. In other cases streptococci have almost exclusively been found.

The bacteria multiplying in a morbid focus increase in virulence,

and when once excited they may reach a certain number of individuals. In this way small epidemics are developed, notably in hospital wards. But what well demonstrates the part played by accessory causes is the fact that individuals with previous lesions of the lung are the only ones attacked.

It is very important to know that, in a certain number of cases, the microbes of the gangrenous focus possess no virulence for animals. The injection into rabbits and guinea pigs of liquids derived from pulmonary gangrene and containing numerous bacteria does not often produce any disturbance. Therefore it seems that, once set in motion, the process continues despite the weakening of the pathogenic agents, which, although capable of causing death in a diseased organism, lose all action when they are transported into a normal body.

The study of pulmonary gangrene has made especially prominent the part played by predisposing causes. Cachexias, diabetes, chronic alcoholism, and inhalation of deleterious gases favour the development of the gangrenous process. The latter may develop at once, or may be consecutive to another pulmonary lesion. From Laennec to Grisolle, it has always been admitted that pulmonary gangrene should not be considered as a consequence of simple pneumonia. Authorities have endeavoured to find signs of differentiation between the two processes, such as more diffuse pain in the side, more intense dyspnœa, and more marked prostration. The distinction was subtle, and has not been confirmed. It is to-day admitted that the pneumonic form of pulmonary gangrene is in reality a pneumonia terminated in gangrene. The statistics of Middlesex Hospital are very interesting in this regard. Out of thirty-four cases of pulmonary gangrene, we find that the process occurred fourteen times in consequence of simple pneumonia, nine times consecutively to cancer of the neighbourhood, and notably to a cancer of the esophagus, six times in the course of chronic pneumonias, four times as the result of embolism, twice in dilatation of the bronchi; lastly, in the other three cases, it was consecutive to cerebral hemiplegia, aneurism of the aorta, and tuberculosis of bronchial ganglia. To complete the etiology, we must add gangrene of traumatic origin and that which supervenes, notably in insane persons, when a bolus of food charged with microbes penetrates into the respiratory passages.

In cases of embolism, it is often a question of transportation of microbic agents started from a gangrenous focus toward the lung. The process is easy to comprehend; the secondary focus is identical with the primary one. But the latter may be simply suppurated: If the pulmonary lesion becomes gangrenous, it is because it is invaded

secondarily by saprophytes, which penetrate with the air and add a putrefactive process to the pyogenic.

A gangrenous focus developed in the lung may reach the pleura by propagation. In other cases *gangrenous pleurisy* will follow a pulmonary abscess, the opening of a tubercular cavity, or as a consequence of the proximity of a tracheal, pulmonary, and especially esophageal cancer. Again, it may be consecutive to suppuration of some distant organ—the liver, the spleen, or the kidney. There is observed in all these cases the development of a sanious, brownish, fetid exudation, comprising the various microbes which we have already seen in the lung. In other cases gangrenous pleurisy may be caused by known microbes—to *Proteus vulgaris* or to *Bacillus coli.*

The abdominal portion of the digestive canal is rarely attacked by gangrene; the superficial necroses of the gastrointestinal mucous membrane are hardly deserving of this name, except in certain cases of dysentery. The true *intestinal gangrenes* are those that recognise a mechanical cause: internal or hernial strangulation permits the invasion of the walls by the numerous microbes of the digestive tube and speedily ends in mortification.

As pulmonary lesions frequently extend into the pleura, so intestinal lesions are often followed by a putrid peritonitis. They may also give birth to emboli, which locate themselves in the liver and there provoke gangrenous abscesses, as is at times observed in the course of dysentery.

Of the other varieties of gangrene, it is convenient to also cite the *swift gangrene of the penis,* which may cause the death of the organ within a few days. The bacteriology of this frightful affection is not known.

Division of Gangrene.—Clinically, two forms of gangrene are admitted—*dry gangrene* and *moist gangrene*—which are related to each other by numerous intermediaries. In dry gangrene, putrefaction is less intense and the odour much less marked. Such is the case in senile gangrene and certain forms of pulmonary gangrene in diabetes.

Chemical analyses have shown that dry gangrene differs from moist gangrene in the smaller amount of water and greater amount of carbon. The odour of the foci is due to the presence of volatile fatty acids, butyric acid, and especially valerianic acid, and of gases, ammonia, and sulphuretted hydrogen. Besides these odorant matters are found leucine, tyrosine, and particularly ferments that seemingly play a very important part. There is one, analogous to trypsine, which digests elastic fibres, and this explains why they are often wanting in the expectoration.

Of the various known or unknown substances contained in a gangrenous focus, some are absorbed and produce the grave phenomena attending the process. It is, as always, a true intoxication of the organism; the general as well as local manifestations of gangrene are explained by the action of the secretions and the microbic fermentations.

Infectious Nodules

In suppuration, as well as in gangrene, it is a question of destructive inflammatory process, without any tendency toward organization. When infection is less violent, the round cells proceeding from the tissues or emigrating from the blood vessels remain living, agglomerate, and constitute little nodules. The latter, in a great number of cases, are not visible to the naked eye; it is the microscope that reveals their presence in the bosom of principal organs—e. g., the liver, spleen, kidneys, and lungs. They form small embryonal productions, which seem to have developed around a microbic colony; but it is not the microbe as a morphological element that acts, since the same lesion may be produced experimentally by injections of toxines.

When the nodule is voluminous and becomes visible to the unassisted eye, it appears under the aspect of granulations that are divisible into two groups: pseudo-typical or nontypical tubercles, which may be produced by the most varied agents, by inanimate foreign bodies as well as by living parasites, animal, vegetable, or microbic; and true tubercles, which are referable to Koch's bacillus and are specific inflammatory nodules.

Tubercles

Anatomical Characters.—Leaving aside the history of pseudo-tubercular granulations, let us consider the development of true tubercles—that is, those caused by the bacillus of Koch (page 109).

From an anatomical standpoint, the tubercle presents itself under three different aspects: gray granulation, Laennec's tubercle, and caseous mass.

Gray granulation is represented by small, hard, protruding, non-enucleable nodosities, often surrounded by a reddish vascular zone. Their dimensions vary from 0.5 millimetre to 2 or 3 millimetres; at first translucent, they subsequently become opaque and yellowish.

Laennec's tubercle is more voluminous; it is a round, gray or yellow mass, having the volume of a pea, a hazelnut, or even of a walnut.

The caseous masses are greenish-yellow deposits, presenting the · aspect of certain cheeses, notably of Roquefort cheese.

These lesions, differing in their macroscopic characters, are constituted on the same plan; they result from the fusion of several elementary lesions designated under the name *tubercular follicles*.

The main characteristic of a tubercular follicle is not such or such a cellular element, but the mutual arrangement of the various elements entering into its constitution.

Theoretically, a tubercular follicle is formed of three zones. In the centre is found a giant cell, the *Riesenzelle* of German authors. Round or polygonal in shape and provided with numerous projections, this nodule contains 20 to 30 oval and nucleolated nuclei, disposed in wreath form in its periphery.

The second zone is composed of epithelioid cells, quite voluminous, with an abundant and somewhat granular protoplasm.

The peripheral zone is represented by embryonal round cells with voluminous nucleus. These cells are very numerous and crowded together.

The various cells constituting the elementary tubercle are united by an intermediary reticulum of a fibrillary nature. Throughout the whole extent of the neoplasm no blood vessel is found, and this is a fact of great importance.

The elementary follicle is not always complete. At first but a mass of round cells is found; at a more advanced period the epithelioid cells may be wanting.

The bacilli are encountered in great number in the giant cells; some are well coloured, others are colourless or surrounded by a capsule. The epithelioid cells often contain one or two of them, but they succumb when a greater number of bacilli penetrate into their interior.

To constitute the various lesions visible to the naked eye, several follicles unite and come to fusion; the agglomeration thus formed represents an individual the centre of which degenerates. A *vitreous degeneration* at first appears; the cells become homogeneous, unite, and form a translucent and fissured mass; then the mass becomes opaque. This is *caseous transformation*, in which morphological elements are no longer perceived, not even bacilli. Around this mass there will again be found the characteristic lesions, the follicles, or the giant cells. So, simply by means of histological examination, Grancher and Thaon have been able to re-establish the unity of tuberculosis, which the studies of Virchow and of Reinhard seemed to have caused to be abandoned. At present there is no longer any doubt in this respect. Villemin has demonstrated that caseous masses as well as granulations give rise to the development of a miliary tuberculosis when inoculated into animals. The discovery of Koch has completed the demonstra-

tion by permitting the detection of the same bacillus in the various anatomico-pathological productions.

The cells entering into the constitution of the tubercle have been considered by some to arise from the fixed cells of the invaded tissue (Baumgarten), and by others to be migratory cells. The latter theory, sustained by Koch and by Metschnikoff, is now tending to prevail. It seems, however, somewhat too exclusive. Histologically, all cells unite to form the tubercle. As regards the phagocytic struggle against the germ, the principal action is referable to the mesodermic elements— namely, to the fixed cells of connective tissue and to leucocytes. The polynuclear leucocytes are the first to arrive, but they rapidly die and are replaced by mononuclear leucocytes, some of which are transformed into epithelioid cells.

As to the giant cell, it is produced either by the hypertrophy of a leucocyte, whose nuclei then increase in number and form a wreath at the periphery of the element, or by the coalescence of several cells. Finally, in certain cases the aspect observed is due to the penetration of leucocytes into a mass of degenerated protoplasm.

Thus constituted, the tubercle progresses toward caseation; it may then soften and open exteriorly. In other cases it undergoes fibrous or calcareous transformation. This is a mode of healing which is expressed by a simple cicatrix.

Localization and Evolution of Tubercles.—Tuberculosis appears in man under very different clinical aspects. Pathogenically, the manifestations that are observed may be grouped under three headings: lesions by inoculation, produced at the point where the bacillus enters the organism, lesions by propagation, and lesions by infection. In the last-named case generalization takes place through the blood; it is the hematogenic tubercles which, contrary to the preceding ones, evolve from within outward. The principal tuberculosis of inoculation is precisely the manifestation that is most frequently observed: common pulmonary tuberculosis. The bacilli introduced with the inspired air, generally protected by the organic particles containing them, ingraft themselves in the apices of the lungs. This localization is to be attributed to the limited expansion of the thoracic cage in the upper parts, and, according to Hanau, especially to the weakness of expiratory movements.

The pulmonary foci, largely communicating with the exterior, are invaded by a considerable number of bacteria, the effects of which are added to those of the principal agent. There occur streptococcus, staphylococcus, pneumococcus, tetragenes, colon bacillus and pneumobacillus, *Micrococcus pneumoniæ* (Ortner), etc. All these agents work to the destruction of the lung, to the formation of cavities; the

soluble products which they produce play a considerable part in the appearance of cachexia and in the development of hectic fever.

The other parts of the respiratory tracts are reached with more difficulty than the lungs. Primary tuberculosis is exceptional in the nasal cavities and quite rare in the larynx. If the current of air passes through the mouth, protection against microbes is still sufficient, and even though the tonsils often contain bacilli at their surface, they are very rarely affected by them.

Next to the respiratory, the digestive apparatus is the most accessible to the bacillus. In most cases, however, the intestinal lesions, as those of the mouth and the larynx, are secondary, and are to be accounted for by the passage or deglutition of expectorations. In the statistics published by the Anatomico-pathological Institute of Munich, out of 1,000 tuberculous individuals, we find 566 cases of secondary tubercular lesions of the intestine, and only 19 of primary lesions. As the aliments are to be accused in the latter case, this etiology is rare in the adult, and more frequent in children who may be nourished with cow's milk containing bacilli.

The existence of intestinal tuberculosis may be looked upon as proved when bacilli are found in the stools; since, in the majority of cases, the microbes swallowed do not pass into the fæcal matters if the intestine is intact. The diagnosis is reached also by the presence of blood in the stools. In cases of tuberculous ulcerations not a week passes without some blood being found in the stools.

Inoculations may also be produced in the skin. The results are local lesions of little virulence, containing few bacilli and manifesting hardly any tendency to generalization. Often primary, these lesions are sometimes due to a secondary inoculation. In a person suffering from common tuberculosis, a particle of expectoration may be accidentally deposited upon a slight abrasion; in other cases, a cutaneous tuberculosis is developed around a tuberculous fistula.

As is known, cutaneous tuberculosis assumes several forms. We may mention the anatomical tubercle; tuberculous lupus; perhaps erythematous lupus, although the last one does not present the histological structure of tubercle, and no bacilli have thus far been found in it; warty tuberculosis of the skin, which is mostly observed in the hands and fingers; and, finally, cutaneous foci. In profoundly affected tuberculous patients, auto-inoculation has been seen to be followed by rebellious ulcerations upon the tongue or the lips, and in cases of intestinal or genito-urinary tuberculosis, in the anus, in the vulva, and in the penis. It is a kind of tuberculous chancre, analogous to that observed in animals experimentally inoculated.

Finally, there remains the genito-urinary apparatus, which may

also be invaded primarily. In the man, the manifestations generally begin in the head of the epididymis, whence the infection spreads successively into the testicle, cords, vesicles, prostate gland, and bladder. At times the bladder or the prostate is reached primarily. In women, the lesions mostly affect the Fallopian tubes, then the ovaries, and the uterus. In both sexes the bacilli may make their way from the bladder to the kidney, and there produce caseous masses and a destructive process extending from the papillæ toward the cortical substance. This aspect permits a distinction between ascending hematogenic and renal lesions. But it is to be noted that genito-urinary localizations that are met with in 1 out of 50 autopsies are in most cases due to a hematogenic origin.

In short, primary or secondary foci of inoculation may be observed in any part of the organism exposed to the contact of the external world. The bacilli, being generally transported by the air, in most cases invade the respiratory passages; the digestive apparatus is more rarely reached, at least in the adult; the skin is quite frequently affected, while primary tuberculosis of the genito-urinary organs is extremely rare.

The focus thus developed may remain isolated, constituting a local lesion, often curable. In other cases it causes inflammation in the neighbouring parts. In the case of organs like the lung, the intestine, the Fallopian tubes, or the seminal vesicles, the adjacent serous membrane may soon be invaded and present manifestations so intense as to dominate all the morbid process.

Nothing in this connection is as instructive as the history of pleurisy.

The investigations of Landouzy, Kelsch and Vaillard, and those more recent of Le Damany, have demonstrated that serous pleurisies, except those depending upon a subjacent pulmonary lesion, are always of a tubercular nature. The liquid contains only few bacilli, and these not constantly; hence its inoculation into guinea pigs rarely produces tuberculosis. On the other hand, it quite frequently contains ordinary bacteria, whose presence does not seem to very much modify the evolution of the process.

Tuberculous pleurisy often assumes a purulent form. The affection is remarkable for its long duration, for the little reaction it provokes, and for the possibility of a chylous transformation. Bacteriological examination is of great diagnostic importance, since by these means it is possible to decide the tuberculous nature of any empyema in which no ordinary pus cocci are present.

The peritoneum, like the pleura, is frequently reached by the tuberculous process. If, in some cases, the propagation is easily followed·

up, and if the lesions of the serous membrane have their origin in previous alterations of the alimentary canal or genital organs, in other cases the peritoneal manifestations seem to be primary. The intestinal route of entrance is cicatrized and can no longer be found, even by an attentive examination.

Tuberculosis may not only propagate by contiguity into the serous system, but also by the circulatory system—lymphatic or sanguineous.

Baumgarten considered as a law the formation of a local lesion at the point where the tubercle bacillus penetrated into the organism. This conception, which is for the most part true, suffers from exceptions. Thus is explained the passage of the bacilli into the lymphatic system from the respiratory tract and from the alimentary canal, and their apparently primary localization in the lymphatic glands. Cervical adenopathies, so frequent in young subjects, develop without our being able to find the entrance of the pathogenic agent.

It is chiefly in the bronchial glands that this fact occurs. In children it is not infrequent to observe very intense tracheo-bronchial adenopathies, with caseous swelling, while the most attentive examination fails to reveal the slightest pulmonary alteration. In some cases the evolution is the reverse of what might have been supposed: the bacilli, having traversed the pulmonary tissue without leaving any trace, reach the glands and there produce extensive lesions and secondarily invade the lung. In such cases pulmonary tuberculosis is consecutive to ganglionic tuberculosis.

Until recently it was believed that facts of this kind are observed only in children. As a result of the researches of Loomis and Pizzini, it is now known that in the adult apparently normal bronchial glands may contain Koch's bacilli. It is hardly necessary to say that this important fact may explain many cases of tubercularization of obscure mechanism.

The same thing may be true with regard to the mesenteric glands, at least in children, since Pizzini has never found the bacilli in these glands in the adult. In children, on the contrary, mesenteric phthisis, or, as it was formerly called, tabes mesenterica, is very frequent, and may develop without any appreciable lesion in the intestine. Experimental pathology furnishes similar facts. In the guinea pig, mesenteric tuberculosis may follow the ingestion of tubercle bacilli without any intestinal lesion.

In other cases the bacilli directly penetrate into the blood circulation, generally after having occasioned a phlebitis, which explains the dissemination of the pathogenic agents. Here two results are possible: The microbes, arriving in small numbers and finding the organism sufficiently resisting, may locate themselves in some organs;

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or, in great numbers invading an organism incapable of destroying them, they may spread throughout the economy and give rise to a general disease, evolving as a pyrexia—namely, *acute miliary tuberculosis*.

In the former case there may be found but a single focus (sometimes a bone only is affected, or an articulation, or a viscus, like the testicle, easily explored). If the initial lesion of the lung has been slight enough to heal, there will be found a focus apparently primary. In other cases it is an ordinary tuberculous individual in whom various organs have been invaded. The liver is almost always attacked at an advanced period of the disease, but its lesions are not generally appreciable except under the microscope. The spleen is more rarely affected. The kidney is quite often attacked, and this hematogenic tuberculosis is expressed by granulations disseminated in its cortical substance, in this way assuming an aspect very different from the one presented by ascending renal tuberculosis.

It is at present admitted that acute miliary tuberculosis is almost always consecutive to a primary focus—i. e., to a cheesy mass, which must be looked for with great care at the autopsy. The penetration of the bacilli is preceded, as already stated, by a specific phlebitis. Weigert was the first to call attention to this mechanism and to show the existence of a tuberculous infection, generally affecting the pulmonary veins and explaining the propagation of the bacilli by a series of microbic emboli. In some rare cases an artery has played the same rôle (Koch).

The bacilli, thus thrown into the circulation, have sometimes been recovered in the blood. Villemin proved the virulence of this liquid, and Weichselbaum, Meisch, Lustig, and Rutimeyer demonstrated the presence in it of the specific agent. The germs deposit themselves in all the organs and tissues, and, according to a great number of accessory circumstances, lodge preferably in one or several organs, which in part explains the different clinical forms observed: typhoid, gastric, latent, bronchial, suffocating, pleural, peritoneal, meningeal, articular, and renal form.

In short, aside from the very rare cases of congenital tuberculosis, the various modes of tuberculous infection may be easily classified in the following manner:

1. Tuberculosis by inoculation, occupying the respiratory passages, more rarely the digestive canal, genito-urinary apparatus, skin, and exceptionally the conjunctiva.

2. Absence of lesions at the point of entrance, or presence of a minute, scarcely perceptible, lesion. In this case secondary localizations are considered as primary.

3. Secondary localizations, whether with or without appreciable primary lesion. The secondary localizations are divided into three groups:

a. Secondary tuberculosis by propagation. The most frequent types are represented by tuberculous pleurisy or peritonitis. In some cases the propagation reaches the osseous system, the biliary passages, and, in case of cutaneous fistula, the skin.

b. Secondary tuberculosis through lymphatic infection, characterized by adenopathies which seem primary and most often occupy the cervical region, where they suppurate quite frequently, and the tracheobronchial or mesenteric glands. In the latter case the affection has been described under the name tabes mesenterica.

c. Secondary tuberculosis through blood infection. This is *hematogenic tuberculosis,* explained by the presence of a specific phlebitis or arteritis; it is expressed either by an external lesion, or by a monovisceral or polyvisceral localization, or by a generalized infection, *acute miliary* or *granular tuberculosis.*

Tuberculosis of Animals.—Tuberculosis constitutes the greatest scourge not only for man, but also for the animals surrounding him—namely, mammals and birds.

Among mammals, those most frequently affected are the *Bovidæ;* the proportion rises to 3 or 4 per cent in the slaughterhouses of the great cities of Europe. The lesions may be reduced to three principal types. Sometimes it is a generalized miliary tuberculosis; in this case the meat is seized. Sometimes it is a local lesion affecting an organ or gland or both; the diseased part is then cut off and the remainder is sold. Sometimes—and this is most frequently the case—it is a pulmonary lesion similar to the human. It appears under the form of voluminous masses, often infiltrated with calcareous salts; in certain cases a whole lobe is involved, weighing 5, 6, and even 10 kilogrammes. In cases of pulmonary tuberculosis, police regulations order the seizure of the affected parts and authorize the sale of the meat.

The most important lesion of local tuberculosis is that of the mammary glands, since the milk then contains bacilli. Fortunately, however, mammary tuberculosis is rather infrequent, and, as in other cases, the bacilli but rarely pass into the milk, the danger of contamination through this secretion seems to have been somewhat exaggerated.

Tuberculosis, rare in the *sheep* and the *goat,* is frequent in the *pig,* where it varies between 0.1 and 1 per 1,000. The *horse* is rarely affected. Contrary to an old opinion, the small rodents, such as *rabbits* and *guinea pigs,* although very apt to contract the disease by inoculation, are almost never attacked spontaneously.

Among domestic animals, the monkey, the cat, and especially the dog, must be cited.

Since the careful investigations of Cadiot, we know that tuberculosis is frequent in the *dog,* but it is not always easily recognised, as the lesions often appear under the form of cancer. The confusion is easy to understand, as microscopic examination may reveal a structure similar to that of cancer. These facts are important to know, for the dog may serve to transmit tuberculosis through his saliva, and especially by his urine, which is often rich in bacilli.

To-day the world agrees in considering all cases of tuberculosis in mammals as due to the same microbe. In consequence of some experimental researches, it was believed that tuberculosis of birds depended upon a special agent, a bacillus of a particular species. This opinion, which has been the subject of much lively discussion, seems to have been finally abandoned. The avian bacillus is nothing but a special variety. It will be considered separately in the *Gallinæ* and in the *Psittaci.*

Tuberculosis of the fowls (*Gallinæ*) is very frequent, since it forms one tenth of the total mortality of aviary birds; it is spread through the excrements, which are rich in bacilli. The infection takes place by the digestive canal, and is expressed by numerous granulations in the liver and spleen. The lesions thus developed are easily inoculated into the rabbit, but with more difficulty into the guinea pig. Reciprocally, tuberculosis of mammals, despite the contrary assertions of writers, may be transmitted to chickens. In accordance with the results of experimentation, inquiries demonstrate that the *Gallinæ* are in most cases contaminated by the expectorations of tuberculous persons.

The histological study of avian tuberculosis leads to quite unexpected results. The tubercle has a special structure, different in animals akin to each other, like the chicken and the pheasant. In the chicken the lesion consists of a vitreous mass bordered by epithelioid cells; in the pheasant it is an accumulation of epithelioid cells limited by a ring of connective tissue, which becomes infiltrated with amyloid matter.

In the *Psittaci* tuberculosis is a frequent affection, generally of human origin, which in most cases is expressed by cutaneous lesions; on the head are seen vegetations, sometimes horns 2 and even 5 centimetres long. At times the lesions occupy the claws, and produce deformities similar to those described as gout of birds.

The bacilli are found in great numbers in the cutaneous productions, saliva, nasal liquid, and excrements; they possess very great virulence for the guinea pig. So tuberculous parrots represent a very serious danger for man.

Finally, there has recently been described a tuberculosis of fish, proceeding from another variety of tubercle bacillus. But these are, at any rate, three varieties of one and the same species.

Nontuberculous Nodular Lesions

Nodular lesions are observed in a great number of infections. In syphilis we meet with gummatous productions which in some respects recall tubercle. We shall not dwell on these lesions, or on those of glanders, leprosy, or fungoid mycosis. They are well known and everywhere well described. Finally, there exists a series of very dis-

PSEUDO-TUBERCULOSES.

- **By inanimate substances.**
  - Cantharides, lycopodium, Cayenne pepper (Martin).
  - Oyster scales (Cornil and Toupet).
  - Stony cells of pears (Hanau).

- **By animal parasites.**
  - Ollulanus tricuspis.
  - Pseudalius ovis pulmonalis.
  - Strongylus vasorum.
  - Strongylus rufescens.
  - Distome.

- **By vegetable parasites.**
  - Oospora bovis or actinomyceta.
  - Oospora farcinosa.
  - Oospora asteroides.
  - Mucor.
  - Aspergillus fumigatus.
  - Aspergillus glaucus.
  - Oidium albicans.

- **Of bacterial origin.**
  - Coccian tuberculosis of the cow (Toussaint).
  - Zoogloeic tuberculosis (Malassez and Vignal).
  - Bacillary pseudo-tuberculosis (Charrin and Roger).
  - Pseudo-tuberculosis (zoogloeic?)
    - of the guinea pig (Zagari).
    - of the rabbit (Dor).
    - of the hare (Megnin and Mosny).
    - of the antelope (Cornil and Toupet).
  - Fetid bacillary pseudo-tuberculosis (Parietti).
  - Bacillary pseudo-tuberculosis of sheep (Preisz and Guinard).
  - Bacillary pseudo-tuberculosis of oxen (Courmont).
  - Human bacillary pseudo-tuberculosis
    - of Du Cazal and Vaillard.
    - of Hayem and Lesage.
    - of J. Courmont.
    - of P. Courmont.

similar facts, which have been embraced under the name pseudo-tuberculosis. In this way are designated all lesions which are characterized by the production of granulations whose macroscopic aspect recalls that of tubercle. The most diverse causes may give rise to them. These are sometimes inanimate substances, more often animate parasites, such as strongylus; comparatively highly organized vegetable parasites, like *Aspergillus fumigatus* or actinomycetes, and finally

microbes. The first example of microbic pseudo-tuberculosis without Koch's bacilli was published by Malassez and Vignal under the name zoogloeic tuberculosis. This affection, which, it seems, had already been perceived by Toussaint, has since been well studied. At the same time numerous observations regarding man and animals have been brought together which seem to establish the existence of several varieties or species of pseudo-tuberculosis. But, following the descriptions, it is not always easy to classify the published facts.

The tabular representations on page 283 will show the great number of pseudo-tuberculoses actually known.

Among the vegetable parasites that may produce lesions similar to tuberculosis a special place is to be given to actinomycetes (page 113). Its introduction into the organism sometimes provokes a special suppuration characterized by the presence of yellow grains, and sometimes the production of tumours similar to sarcoma.

Very frequent in *Bovidæ,* where it is encountered in the proportion of 5 per cent (Russia, Germany), 8 per cent (England), 1 per 1,000 (Lyons), 0.7 per 1,000 (Paris), actinomycosis is not absolutely rare in man. Contamination occurs by contact of diseased animals, more often as the result of penetration beneath the skin or in some mucous membrane of a spike of grain or barley on which the parasite vegetates. It is mostly about the mouth that infection takes place; it is favoured by the presence of carious teeth.

According to its location, the parasite gives rise to various manifestations. There have been described cervico-facial, thoracic, abdominal, cerebral, cutaneous, and pyæmic forms. The phenomena recall those of tuberculosis or syphilis. Confusion with the latter disease is easy, as in both cases iodide of potassium exerts a specific action.

The clinical analogy with tuberculosis is confirmed by bacteriology. We have already cited numerous researches tending to demonstrate that the bacillary form of the tubercular microbe is but a transition form, and that in certain conditions the parasite assumes a special aspect, similar to that of actinomyces.

CHAPTER XV

SEPTICÆMIA AND PYÆMIA

Definition of the terms septicæmia, pyæmia, bacteriæmia, bacterio-toxæmia—
Cryptogenetic, consecutive, and secondary bacteriæmia—Septicæmic forms of
infections or specific septicæmia—The agents of septicæmia and pyæmia—Ana-
tomical distinction between the two processes; clinical and bacteriological
analogies—Etiological division of septicæmias and pyæmias—Principal clin-
ical characters—Evolution—Importance and frequency of attenuated forms.

Definition and Division of Septicæmia and Pyæmia.—Septicæmia
and pyæmia constitute two morbid processes, which must be drawn
nearer and united under the name *bacteriæmia.* In fact, the patho-
genic agent tends to invade the entire organism and to develop there
without causing special lesions (septicæmia); or it locates itself in
certain viscera or tissues and gives rise to the formation of purulent
foci (pyæmia). In the latter case a considerable number of small
abscesses are generally found, at the autopsy, occupying the liver, kid-
neys, lungs, heart, etc. These are designated by the quite improper
name *metastatic abscesses.*

Bacteriæmia must be distinguished from *bacterio-toxæmia,* in
which the pathogenic agent remains localized and excites general dis-
turbances by means of the toxines it secretes. In bacteriæmia there is
general infection; in bacterio-toxæmia, intoxication.

Bacteriæmia therefore includes both septicæmia and pyæmia. The
expression *septicæmia,* created by Piorry, was applied by him to every
alteration produced in the blood by septic or putrid matters, whatever
their origin. After having been employed in most diverse senses, the
term was adopted by bacteriologists, who have not been able to offer
any better definition than clinicians. Confusion was further increased
when the bacillus of gaseous gangrene was called *septic vibrio,* and the
disease induced by it *gangrenous septicæmia.* These inaccurate terms
led to great errors and nosological confusion. Thus, for example,
deceived by these words, some authors believed that septicæmia and
pyæmia should be separated on the ground of the different characters

of their pathogenic agents. Following the expressions used by bacteriologists, they believed that the former of these two processes was due to an anaërobic bacillus—i. e., septic vibrio—remaining at the point of introduction; the latter to aërobic microbes invading the organism, and there producing secondary abscesses.

A word evidently having no other sense than that given it by an author may be employed, provided it be well defined. The term septicæmia, then, might be reserved for gaseous gangrene and similar processes. This, however, would be a notable departure from the prevailing tendency, as logically it would be necessary to consider all local diseases which kill by intoxication as septicæmia, and also to include tetanus, diphtheria, cholera, etc., in this group. In these infections, as in gaseous gangrene, the microbes remain localized at one point, and it is their soluble products that excite general reactions. The disease is therefore of a toxic nature. This is why these diverse processes constitute a separate group—i. e., bacterio-toxæmia—and why gangrenous septicæmia must be excluded from the group of true septicæmias.

Thus limited, bacteriæmia represents a nosological class, which is as yet artificial. Nevertheless, its existence may be justified by the following considerations.

In cases of septicæmia the microbe is present in every part of the organism. It may often be detected in the blood during life, and always after death. The lesions are those common to all intense infections. The blood is disintegrated and dark in colour; numerous ecchymoses are observed in the viscera and tissues. At times hemorrhages are so abundant that the process deserves to be designated as *hemorrhagic septicæmia*. The microscope reveals small vascular thromboses, cellular degenerations, and occasionally embryonic foci, indicating a reactionary tendency on the part of the organism. These foci, however, are limited, and are not visible to the naked eye.

At the end of a variable time, however, the microbes become localized in certain portions of the economy. Septicæmia then loses the character of a general infection, and visceral localizations become prominent. Consisting at times of simple inflammatory lesions, the secondary foci may, in other instances, undergo purulent transformation. Under these circumstances the process is sometimes called *septico-pyæmia*, which represents a transition with pyæmia properly so called.

Pyæmia is distinguished from septicæmia by the tendency of the infectious agent to localize itself from the beginning in certain viscera or tissues, and there give rise to the formation of purulent foci. The pathogenic agent transported by the blood quickly leaves this

medium; hence certain authors admit that in true pyæmia the microbes are encountered exclusively in the tissues. When they are found at the same time in the blood the process is known as septico-pyæmia. We will soon see that this last distinction is of a rather subtle nature.

Septicæmia and pyæmia may produce anatomical lesions, and they may also be consecutive to some local lesion. According to their apparent point of departure, two varieties may be admitted. The first is characterized by invasion at once of the entire organism; the point of entrance of the microbe and the initial lesion are wanting or remain unperceived. Under these circumstances the infection is said to be *spontaneous* or *cryptogenetic*. The latter terms, introduced by von Leube and accepted by Jürgensen, is now frequently employed in Germany. In the second case general infection is preceded by a local lesion. Here two events are possible: Sometimes the primary focus contains the microbes which will invade the economy, in which instance bacteriæmia deserves the name *consecutive*. Sometimes, on the other hand, the primary focus is due to specific or nonspecific agents, which only prepare a route of entry for the microbe of general infection, in which case bacteriæmia is said to be *secondary*.

According to the few considerations just presented, we may classify the various types of septicæmia and pyæmic infections as follows:

CLASSIFICATION OF SEPTICÆMIAS AND PYÆMIAS

According to their Origin.	*According to their Evolution.*
Primary . . . . { Traumatic. Cryptogenetic.	Without special localization (true septicæmias). With inflammatory visceral localizations.
Consecutive. Secondary.	With suppurative { Septico-pyæmias. localizations. { Pyæmias.

It may be asked whether general infection is not always consecutive to a local lesion which in some instances is so minute as to escape detection. Such an occurrence is frequent, but the reality of primary general infection seems demonstrated by numerous surgical observations and experimental researches. Clinically, disturbances have been seen to follow an accidental, an operative, or an obstetrical wound which seemed perfect. It is the same with animals. When an extremely virulent microbe—a certain streptococcus, for example—is inoculated beneath the skin, death supervenes from bacteriæmia without there being any trace of local lesion. Furthermore, under a very great number of circumstances, the microbes located upon or within our bodies, notably those of the digestive canal, may penetrate

into the economy, and, if the system is sufficiently weakened, it is comprehensible that they may at once create a general disease. In such cases it is impossible to find a trace of their passage. No local lesion exists. If it were always possible to determine the mechanism of the infection, facts of this kind should be grouped under the name *auto-bacteriæmia.*

Consecutive general infections, however, are the most frequent and important, since they include the great majority of surgical and obstetrical septicæmias and pyæmias. With these must also be included certain cases in which the primary lesions are of a medical order—i. e., occupying such parts of the organism and affecting such localities as to render operative intervention impracticable.

It is not alone in suppurative lesions that this process is called into play. It is of constant occurrence in the course of the most diverse diseases. In this way, when an erysipelas or a plain pneumonia terminates in death, the infection nearly always assumes a septicæmic form. At the autopsy, and even during life, the microbe—streptococcus or pneumococcus—is found in the blood and all the organs.

The same evolution is observable with highly differentiated bacteria. For example, this takes place in anthrax. In man, the bacillus produces a local lesion—i. e., a malignant pustule. It too often crosses the barrier opposed to it by the organism and invades the entire economy. It is then said that the patient has died by anthrax septicæmia. It may even happen, at least in animals, that the local lesion is wanting. In such cases anthrax manifests itself as a true septicæmia.

It is even said that such or such an infection assumes a septicæmic form in cases in which it develops without occasioning its usual manifestations or lesions. Thus, a septicæmic form of typhoid fever has been described. It would therefore be easy to extend the limit of septicæmias so as to include almost all infections, at least in certain forms.

To avoid the confusion which would result from such a conception, we are obliged to arbitrarily designate as septicæmias those bacteriæmias that are due to ordinary agents, and to distinguish those cases in which a well-defined agent has from the first or consecutively invaded the entire organism and behaved as in true septicæmia, as septicæmic forms or *specific septicæmias.* Thus, to take up the examples above referred to, we shall speak of a septicæmia with streptococcus and a septicæmia with staphylococcus; whereas, if the case be one of general infection by the *Bacillus anthracis,* we shall make use of the expressions specific septicæmia or septicæmic form of anthrax. By so

doing we conform alike to clinical data and to the results of bacteriology.

We believe it proper sharply to separate the consecutive from the secondary infections. The distinction is equally justified by clinical experience and bacteriology. In consecutive infections the same microbe produces all the lesions. Let us take, for example, a purulent infection consecutive to a phlegmon. Clinically, it is the same process that has become generalized. Bacteriologically, the same microbe —staphylococcus or streptococcus—is found in the initial phlegmon and in the metastatic abscesses. Pyæmia is then said to be consecutive.

On the other hand, let us assume that a diphtheritic angina exists. If the patient succumbs to septicæmia, we may say that this septicæmia is secondary, as the latter will be produced by streptococcus, while the primary agent has remained localized in the throat. The process is one which has been secondarily superadded to the primary. Likewise, the arthrites of gonorrhœa may sometimes be produced by the gonococcus. Here the process is one of generalization due to the main infection, viz., a consecutive bacteriæmia. More often these arthrites are due to an infection superadded by a pyogenic agent which has simply profited by the urethral lesion and invaded the economy. This is a secondary bacteriæmia.

Bacteriology.—It has seemed to us useful to unite septicæmia and pyæmia in one group. Although pathological anatomy sharply separates these two processes, clinical observation justifies their closer relation, and bacteriology confirms the results of observation by establishing that the same pathogenic agents are concerned in the majority of cases.

There exist a few microbes which thus far have been met with only in one of the two processes. This, however, is the exception. What is most often detected in cases of septicæmia or pyæmia is, first, streptococcus, then *Staphylococcus aureus*, more rarely pneumococcus, pneumobacillus, or tetragenus. Among the other septicæmia agents we may cite the colon bacillus, bacillus of psittacosis, bacillus of hemorrhagic septicæmia (important chiefly in animals), *Bacillus pyocyaneus, Bacillus septicus putidus, Bacillus proteus vulgaris,* etc. The agents of pyæmia are much more numerous. Besides the microbes already mentioned, we shall note a special bacillus described by Levy. Parasites of a higher order, such as actinomyces, might also be cited; also the bacillus of glanders, which causes a true specific pyæmia justly described by authors in a separate chapter.

General Etiology.—From a purely etiological standpoint, septicæmias and pyæmias are divided into puerperal or obstetrical, surgical, and medical.

The streptococcus, which, as we have said, plays the principal part, is the almost constant agent of puerperal septicæmia and pyæmia. Clinical experience has prepared us for the acceptance of this fact revealed by bacteriology. Puerperal fever has more than once been contracted by patients treated in proximity to erysipelatous women. On the other hand, erysipelas has at times appeared in persons who had taken care of puerperal women. Finally, there are cases in which the two infectious manifestations coexist in the same subject. However, the bearing of these facts should not be exaggerated. Women suffering with erysipelas have often been confined without developing septicæmia, and erysipelas has appeared a few days after confinement and been perfectly cured.

Contamination occurs mainly from one to another puerperal woman. The streptococcus then proves to be much more active, and seems to be endowed with special virulence. It is in such cases that infection may be transported to a distance through the agency of clothing, linen, and instruments.

Lastly, the infection may appear spontaneously. It is explained by an auto-infection due to microbes normally inhabiting the external genitals.

We shall not dwell upon the causes of surgical infections. Three conditions may be present. Sometimes, the wound being soiled by germs, general infection is established at once; sometimes a local lesion is first produced, which subsequently induces a general infection; finally, infection follows a traumatism without there being any external wound. Facts entering into this last category are exceptional. Wagner has recorded a remarkable example in a case of pyæmia consecutive to a fall upon the hip.

When bacteriæmia is consecutive to a wound it is not at all necessary that the latter be extensive. Disturbances have been seen to occur in consequence of minute traumatisms. Dandois has reported a case in which pyæmia followed a leech bite. It should be remembered, however, that infection is always favoured by all causes producing great damage and profound attrition of the soft parts. Disinfection of such wounds is difficult, and the microbes find conditions favourable for their development in the altered and contused tissues. Finally, in surgical as well as puerperal infections, the dominant etiological factor is the transportation of germs by the hands of the operator or through badly sterilized instruments.

At the present day these are commonplace facts, and need but to be mentioned.

The last group, which belongs to the domain of both surgery and medicine, includes the cases in which bacteriæmia is consecutive to

some old lesions. These are suppurating wounds, oftener profound suppurations, whose disinfection is a difficult matter. We have already shown in connection with suppuration that, in order to explain the generalization, it was necessary to assume a previous modification of the organism, probably under the influence of microbic products originating from the primary focus.

We are, of course, unable to cite all the lesions that are liable to terminate in a general infection. Cutaneous or superficial alterations rarely have this effect, except in the newborn, in whom suppurations of the umbilical cord cause an omphalitis permitting microbic generalization. In adults, suppurations within cavities or the viscera are especially liable to give rise to general infection. It is true, however, that since the general adoption of antisepsis the number of cases of infection is constantly diminishing. In cases of otitis, for example, Chauvel found, out of a total of 1,137 observations, but 5 cases of septico-pyæmia, only 2 of which proved fatal.

Likewise, in *medical affections* there is no constant relation between the gravity of the primary lesion and its tendency to generalization. Cutaneous suppurations, notably those of smallpox, alterations of the tonsils, intestinal ulcerations, lesions of the liver, urinary passages, and the lungs, are the most frequent causes of the infective process.

The primary lesion is not necessarily suppurative. Diphtheritic or scarlatinal sore throat may open the door to pus cocci. We must give a special place to common infections, which are so frequently observed in the course of tuberculosis and which modify the progress and aspect of the disease. In examining during life the blood of patients attacked by febrile phthisis, Jakowski found microbes seven times: *Staphylococcus aureus*, five times, twice in a pure culture, twice associated with *Staphylococcus albus*, once with streptococcus; in the other two cases he discovered streptococcus. In an observation of Étienne and Specker, tuberculosis was complicated with a septicæmia induced by a microbe related to the pneumococcus. These secondary infections play a great rôle in the mechanism of hectic fever, and in other cases may give rise to multiple suppurations, purulent arthritis, and visceral abscesses.

Lastly, there remains the group of *cryptogenetic septicæmias*, in which general infection seems to supervene at once. This group may be divided into two secondary groups. At times the initial lesion passes unnoticed. During life it is not revealed by any appreciable symptom, but none the less it exists, and is found at the autopsy. It may be a visceral suppuration, an intestinal ulceration, an old focus having its seat in a ganglion, or a suppurative salpingitis, etc.

In other cases, on the contrary, the minutest post-mortem examination fails to reveal any internal lesion. Infection is produced from the beginning. In a good many cases it is explained by a previous weakening or decline of the organism. In fact, it is known that, on the slightest occasional cause, the germs which multiply upon the integuments or mucous membranes invade the economy. It is even probable that they constantly penetrate into the tissues under normal conditions. But those which enter a healthy organism are rapidly destroyed. It is no longer so, however, when the organism suffers from the influence of an accessory cause—for example, cold, fatigue, or overwork. The part played by overwork seems to us very important, and the clinical cases known under the name *overwork fever* (*fièvre de surmenage*) must be considered as septicæmic. Excessive muscular work facilitates infection by lessening the alkalinity and diminishing the germicidal power of the humours. Infection occurs through the skin, perhaps more frequently through the intestinal mucous membrane. It is known with what facility germs pass through the walls of the digestive tract. Fæcal stagnation, during only five or six hours, suffices to produce general infection (Arnd, Multanowski). It is then probable that a good many infections whose point of departure escapes our notice must be referred to an intestinal origin.

However, it must be acknowledged that there are cases which defy all explanation. No cause whatever is found permitting us to understand their development.

Evolution.—Infection may behave throughout its course as a septicæmia without any localization. The characteristics of the disease are severe initial chills, high fever, and a very grave general state. If the evolution is rapid, death supervenes without any organ being especially affected. If the disease be prolonged, visceral localization may occur. General manifestations then become less, and the lesion which expresses the fixation of the process develops on its own account. There exist numerous transitions between pure septicæmias and those where general infection, pushed into the background, may become so slight as to be hardly noticeable. And yet septicæmia has been an intermediary state between the primary lesion and the secondary localization in some viscus. Acute endocarditis, nephritis, or hepatitis are in many cases but septicæmias with a predominant localization.

If the visceral localizations of septicæmia are expressed by the production of purulent foci, it is said that septicæmia terminates in pyæmia. In other cases pyæmia comes on at once. It is difficult to say why, under certain circumstances, a septicæmic agent gives rise to suppuration. The consensus of opinion assumes that, in the latter

case, it is less virulent. Septicæmias seem mostly to be of a toxo-infectious nature. They occur when bacteria find in the organism conditions favourable for the production of toxines. In contrary cases they are in part destroyed, and the proteines of their cadavers cause the formation of pus.

Pyæmias, primary or secondary, are expressed by multiple suppurations, which sometimes occupy superficial regions—skin or articulations—sometimes the viscera. The medical pyæmias with articular localizations, long confounded with acute articular rheumatism, have been described under the name *arthrito-suppurative disease* and *infectious pseudo-rheumatism*. The lesions have a great tendency to localize themselves in some joints and to induce suppuration and anchylosis.

Pyæmias with cutaneous and subcutaneous determination are less frequent. In the former case infectious erythemata, purpura, pustules, and bullæ full of pus develop; in the latter case, multiple phlegmons appear.

It is also to pyæmia that German writers attribute the osteomyelitis of adolescents. This conception is perfectly acceptable, as it explains the gravity of general phenomena, and, as is often observed, their attenuation when localization of the process takes place. Accordingly, osteomyelitis would be staphylococcic pyæmia of young subjects.

As to visceral pyæmias, they are too well known to need a study here. Multiple abscesses are found chiefly in the kidneys, liver, spleen, lungs, and brain; and purulent collections in the serous membranes, purulent infiltrations in the heart, etc. It is not rare to see these various forms associated. In the ordinary surgical pyæmia foci exist simultaneously in the viscera and the joints.

Attenuated Forms of Septicæmias and Pyæmias.—The expressions septicæmia and pyæmia immediately suggest the idea of a grave and most often fatal process. However, along with the acute forms, we must admit a certain number of cases where the process becomes localized and tends to resolve. At times the manifestations may even be ephemeral. Traumatic fever and milk fever are nothing else than septicæmic fevers, so innocent that they may pass away within twenty-four or forty-eight hours. It is the same with certain urinary fevers, which have but a transitory duration. In other instances the evolution, which had at first seemed very serious, becomes modified at a certain moment. This takes place when a visceral localization occurs. In the course of a puerperal septicæmia, for example, the disquieting manifestations will decrease and disappear when a phlebitis or a peri-uterine purulent focus develops. The lesion seems to be a point of

attraction for the circulating microbes, and it is conceivable that certain authors, like Dr. Fochier, should have proposed to suppress the infectious process by attempting to localize them by means of fixation abscesses.

The same remarks are applicable to pyæmias. While the generalized forms—those, at least, where numerous visceral foci exist—are inevitably fatal, there exist benign pyæmias in which localization takes place in a tissue—e. g., in a joint. These cases can be cured after surgical intervention.

In conclusion, along with acute generalized septicæmias it is convenient to admit attenuated forms—transitory septicæmia (milk fever); innocent septicæmia with subacute or chronic course; septicæmia with a single secondary localization, suppurated or not; pyæmia with a single or very few localizations. These various forms easily terminate in recovery. Even in grave cases the prognosis is not always fatal. There are on record cured cases of generalized infections. This fortunate result is observed chiefly in septicæmia because the latter is not attended by profound cellular lesions. In the case of generalized visceral pyæmia, the attenuation or even destruction of the agents is of no consequence. The patient will succumb, not to the infection, but to the visceral lesions resulting therefrom.

CHAPTER XVI

EVOLUTION OF INFLAMMATIONS—SCLEROSIS

Alterations of epithelial cells; their degeneration—Proliferation of epithelial cells
—Adenoma—Functional disturbances—Reparation of lesions—Sclerosis—Sig-
nificance of the sclerotic process—Mode of formation of scleroses—Arterio-
sclerosis; importance of this process; principal clinical forms—Notions of
therapeutics.

Alterations of Epithelial Cells.—In the study which we have thus
far made of inflammation, we devoted our attention especially to the
elements of connective tissue—namely, elements proceeding from the
middle layer of the blastoderm. We have seen that these elements
undergo two sorts of modifications—namely, phenomena of degenera-
tion, which are not very pronounced, and reactionary phenomena,
which are very intense and terminate in the production of various
cells that are found in the exudations. We have also shown that
proliferation is not a wholly local process. On the contrary, the entire
organism becomes impregnated in consequence of the absorption of
toxic products. Modifications also occur in the various tissues con-
cerned in the production of leucocytes—i. e., in the spleen, lymphatic
glands, and bone marrow.

The changes produced in the epithelial cells are of an analogous
nature, except that, contrary to what occurs with the mesodermic tis-
sues, degeneration predominates over proliferation. These phenom-
ena of degeneration are especially marked at the inflamed point, and,
if the lesion be prolonged, they may be observed in distant parts and
reach the principal viscera. Here, again, the question is one of a
toxic process, of absorption from the focus of soluble substances, which
induce various degenerations in the economy, notably fatty or amyloid
degeneration.

In its highest expression, the damage done to the vitality of the
cells is manifested by the process designated by Weigert as *coagula-
tion necrosis* or *fibrinous degeneration*. The cell is transformed into
a small, dry, fragmented mass, similar to coagulated fibrine; the

nucleus disappears, and nothing remains to recall the original structure.

If the inflammation is less intense, a series of degenerations occurs, which we shall briefly indicate. First of these is fatty degeneration—namely, the production of small drops of fat in the protoplasm of the cell. This process, which is very clearly shown in the liver, kidney, and myocardium, should not be confounded with fatty infiltration. In the latter process a drop of fat is deposited in the cell and crowds the protoplasm, but the latter retains its vitality and functional activity. In fatty degeneration the protoplasm itself undergoes metamorphosis.

Fatty degeneration is also indicative of an acute process. In less intense grades granular degeneration characterized by a cloudy metamorphosis of the protoplasmic albumin, is observed, also colloid, vacuolated, hyaline, and amyloid degenerations, the latter especially frequent in the vascular system; mucoid degeneration, and, finally, pigmentary degeneration. All of these lesions will be discussed in a special chapter.

While these various modifications are produced in the cell, changes of no less importance occur in the nucleus. If the process is very intense, as in coagulation necrosis, the nucleus disappears; if less intense, the nucleus atrophies, and in other cases it proliferates. This last modification is observed when the inflammation is not too intense, and it is also encountered at the periphery of the lesions—i. e., around the parts which degenerate and become necrosed.

Cellular reactions may differ in the same organ, according to the system concerned. In the liver, for instance, the toxic or infectious substances produce degeneration of the hepatic cells, while the epithelia of the bile passages proliferate. The explanation is that the supporting cells of the excretory ducts are not as highly organized as the secretory cells; consequently, they are less delicate and more resistant. This is why a production of newly formed biliary canaliculi is observed along with degeneration of the hepatic cells in certain infections of the liver.

If the inflammation is subacute or chronic, the hepatic cells themselves may proliferate. In this way nodules are formed, the cells of which are grouped in such a manner as to constitute small tumours, sometimes described under the name *adenoma*.

In slow inflammations of the skin and mucous membranes, hyperplasia is also observed. In chronic gastritis, enteritis, or metritis the glands become elongated, develop, and form small tumours. In this manner are produced adenomata, which constitute a transition between inflammations and neoplasms.

The various alterations produced in the inflamed cells modify their volume, form, mutual relations, and functional activity. When degeneration is predominant, the cell, which at first may be hypertrophic, atrophies, and is no longer represented except by small, unrecognisable, cuboidal elements. When proliferative reaction predominates, the cell grows and hypertrophies. These changes of volume may of themselves modify the normal disposition of the tissues. On the other hand, the functional disturbances produced hinder the production of the cement substance which unites the cellular elements. This lesion, first described by Drs. Landouzy and Renaut, is especially easy to study in the myocardium. The various cells of the myocardium become dissociated and undergo segmentation. The process in the liver is probably similar to segmentary myocarditis, and explains the dislocation of the hepatic elements observed in grave infections of the liver.

It can readily be understood that these various lesions lead to a profound modification of the functional activity of the cells. If the inflammation is very intense, function is abolished and secretion is arrested or considerably diminished. If, on the other hand, the inflammation is slight, the epithelia are stimulated and secretion is increased, but the latter deviates from the normal type.

In this manner are developed catarrhs characterized by the production of abundant fluids rich in mucine and containing numerous altered cells and colloid exudates derived from diseased elements. It will suffice to recall what takes place in the stomach, intestine, biliary passages, and especially in the kidneys. In the various forms of nephritis, for example, the urine contains numerous cells, isolated or united in cylinders, or exudations which are moulded in the tubules and constitute the so-called hyaline casts.

Reparation of Lesions.—The alterations we have just indicated may resolve and disappear. Reparation, however, is seldom perfect; for whenever the process attains a somewhat intense character the affected cells disappear and are replaced by cicatricial tissue.

There is a very curious difference between the evolution of traumatic lesions and that of inflammatory lesions. The former are repaired with the greatest facility. Experimenters and surgeons have shown that the viscera regenerate. In animals it is possible to remove large portions of the liver, spleen, or kidneys. In such instances the mutilated organs are reproduced according to their normal type. The directing idea presiding over the development of the individual seems sufficiently strong to assure restoration and a return to the original or normal condition.

The destruction of cells is often much less marked in inflammation than in traumatisms. The lesions are less extensive and less consid-

erable. In certain cases but a few cells are destroyed; their reparative work seems easier, and yet it does not take place. The directing idea seems to have been inactive.

The paradox distinguishing these two orders of facts may be compared to that offered by the study of heredity. We have seen that accidental traumatic mutilations are not transmitted to the offspring. On the contrary, lesions consecutive to functional disturbances are generally inheritable. The cause which has induced an anatomical alteration by producing a physiological change has been strong enough to modify the law of preservation of the ancestral type. That which appears so clearly concerning the succession of beings is also applicable to the individual. Traumatic lesions are accidents which do not modify the normal evolutive type; they may be repaired in the subject, and do not influence his descendants. On the other hand, anatomical lesions dependent upon some functional disorder express an impregnation of the economy by a pathogenic agent; they are responsive manifestations resulting from a change in the organic direction, are repaired incompletely and with difficulty, and are transmitted by heredity. This is a new proof that the great laws which govern the life of the individual are the same as those which govern the life of the species.

Reparation takes place through the agency of the cells which have proliferated, chiefly the mesodermic and the migratory cells. In this way buds are formed which become vascularized. Sometimes the appearance of blood vessels is explained by the development of a vessel-forming cell, which communicates with neighbouring capillaries by means of prolongations. Sometimes solid cords are observed, which subsequently become hollow and join the capillaries. Most frequently, however, the capillaries themselves send out ramifications toward the tissues and re-establish the circulation.

The cells increase in number through the supply of nutritive materials furnished by the newly formed vessels. The differentiated elements are reproduced, and clasmatocytes reappear. Finally, the parts that can not be reconstructed according to the normal type are replaced by fibrous connective tissue. This is sclerosis.

SCLEROSIS

Well-constituted sclerotic tissue is feebly vascular. It is white, hard, resistant, and grates under the scalpel. Sometimes it is exuberant and gives to the viscera in which it occurs an exaggerated development. Such is the case with hypertrophic cirrhoses. Sometimes it appears under the form of a tumour—i. e., keloid. On the other hand, it sometimes manifests a notable tendency to retraction and to diminish

the bulk of the organs. If it occurs in a canal, it causes a progressive stricture, as, for example, in the esophagus and urethra. When it develops in a viscus, the sclerotic tissue leads to atrophy of the organ. The compressed soft parts protrude and impart a granular aspect to the organ. This fact explains Laennec's granulations in atrophic cirrhosis and Bright's granulations in interstitial nephritis. Simultaneously with the evolution of these lesions, the parts that have remained healthy tend to replace the diseased parts. In this manner hyperplasias and compensating hypertrophies are produced which further modify the form of the organ.

Sclerotic tissue may have other disadvantages. By lining parts which should unite, it may become the cause of fistulæ; when it develops in parts anomalously in contact, it may give rise to adhesions. In other cases it causes vicious cicatrices and disturbs the functional activity of the organs. It compresses subjacent parts or it narrows the vessels supplying the organs, and thus interferes with their nutrition.

Sclerotic tissue, therefore, fills up the vacant spaces left by degenerated and dead cells. In other words, it is a substitution tissue. To a certain extent sclerotic tissue represents a conservative lesion, no matter whether it develops, as is generally admitted, at the expense of connective-tissue cells—i. e., is preceded by an embryonal stage—or progressively through hypertrophy of pre-existing fibres, as in certain cases seems undeniable; or, according to the recent views of Retterer, as the result of a transformation of ectodermic and endodermic cells. However, while it remedies the primary accidents, it at the same time becomes the cause of new disturbances. It may be said, therefore, that sclerosis is both an end and a starting point.

Sclerosis is the last stage of all pathogenic causes that have entered into the life of the individual, and this explains its great frequency in the aged. Exogenous intoxications, acute or chronic intoxications, auto-intoxications, including overwork, nutritive disturbances, and, above all, arthritism, are justly regarded as etiological factors in its production.

Several of these same causes may induce cellular degenerations without sclerosis. In the liver, for example, alcoholic intoxication sometimes gives rise to diffuse steatosis, and sometimes it causes cirrhosis. The same is true of infections. For example, tuberculosis produces either fatty degeneration, hypertrophic cirrhosis of the liver, or an atrophic cirrhosis comparable to that observed in drinkers.

The different effects produced by the same etiological conditions cited in the chapters devoted to degenerations and scleroses are explained by the varied degree of power possessed by the pathogenic

agent or by a dissimilar responsive aptitude on the part of the organism.

When the cause is very active or the organism weakened, degeneration predominates; when, on the other hand, the cause is less active or the organism more resistant, sclerosis prevails. Tuberculosis causes degeneration in predisposed individuals; in subjects but slightly sensitive to this infection; in arthritics, for example, it manifests a tendency to produce fibroid changes. The same holds good in regard to intoxications. For example, alcohol, when administered in large doses, causes fatty degeneration; in small doses it produces cirrhosis. It has been possible to produce either of these processes in animals by giving similar doses of this poison. In order to obtain degeneration or sclerosis at will, all that is necessary is to place the subjects experimented upon under good or bad hygienic conditions and to furnish them copious or insufficient nourishment. This has been realized with phosphorus in the case of the liver, and with cantharides in the case of the kidneys.

Epithelial Origin of Sclerosis.—The preceding facts force us to admit that sclerosis is the cicatrix of cellular lesions, and lead us to reject the existence of primary scleroses. The consecutive tissue alteration is always preceded by a lesion bearing on the more highly organized elements. Scleroses, therefore, are always of epithelial origin.

For example, let us take an organ in which scleroses have frequently been studied—namely, the kidney. Two types of nephrites were formerly admitted, some epithelial, others interstitial—i. e., sclerotic from the beginning. To each of these affections a different etiology, pathogenesis, and symptomatology were assigned. Little by little a change was wrought. It has finally become recognised that every nephritis starts with the epithelial elements, and that the process soon extends, so that nephritis is primarily diffuse and subsequently advances toward different anatomical types, the two extremes of which are represented by the large white kidney, where epithelial lesions predominate, and by the small, contracted red kidney in which sclerotic lesions prevail. Thus are produced sharply distinguished affections, which must be separated in anatomical and clinical descriptions. The starting point, however, is the same, but the final result differs because organisms are not similar.

The same conception is applicable to hepatic cirrhoses. The origin must be looked for in a primary lesion of the hepatic or biliary cells. The still classical idea which attributes atrophic cirrhosis to a primary alteration of the portal vein or to a periportal cirrhosis is based upon incomplete anatomical study. It is now demonstrated that the process is not as systematic as was formerly supposed. Sclerosis de-

velops simultaneously around the portal and hepatic veins and forms aberrant bands, defying all topography. On the other hand, a sclerotic lesion is never seen to radiate toward neighbouring parts. It is probable, then, that poisons and microbes carried by the portal vein give rise to primary alterations in the hepatic cells. The marginal cells are the first to be reached and the most profoundly affected. Next to be attacked are the centrally located cells in the region where the blood which has passed through the radiate capillaries enters the central vein. In this way the topography of sclerotic lesions is explained. As to the venous alterations, they seem most frequently to be secondary. It may, however, be admitted that they are sometimes primary, in which instance they produce sclerosis because the disturbances of circulation alter the nutrition of the cells. Even in this case the sclerotic process is not an irradiation of the periphlebitis; on the contrary, it is consecutive to a degenerative alteration of the hepatic cells.

When the question is one of biliary hypertrophic cirrhosis, there can then be no doubt as to the primary lesion being located in the cells. It affects the epithelia of the biliary passages and seems to be caused by the colon bacillus coming from the intestine.

It would be easy to present analogous examples with respect to other glands and various tissues. Therefore, sclerosis always comes to fill up a vacant space.

Scleroses of the nervous tissue form no exception, since it is now known that scleroses of the neuroglia do not enter into the group of true scleroses. The neuroglia does not represent connective tissue; it is of ectodermic origin and a nervous tissue. It is not strange, therefore, that it should be the seat of systematic lesions to which the rules here laid down do not apply. It is a special process quite different from true mesodermic sclerosis.

Arteriosclerosis.—Instead of being localized at a certain point, as in the preceding examples, sclerosis may be generalized, or at least distributed to a great part of the organism, affecting especially the vascular system and attacking several viscera at once.

It is to the history of this morbid state that the law which we have above formulated especially applies. Arteriosclerosis is truly the last stage of all morbid, infectious, or toxic causes which have acted during life. The reason why the arteries are so often affected at a relatively early age and at a time when the organs are still quite healthy is that they serve to carry microbes and toxines and are constantly contaminated by noxious substances. The most highly organized elements of the vessel walls, notably the muscle fibres, degenerate and sclerosis is produced.

Arteriosclerosis, which may commence at an early age, is almost never absent in the aged or even in adults. There are records of men whose arteries were supple at the age of eighty or ninety years. Such instances, however, are very rare. More frequently arteriosclerosis is manifest as early as the thirtieth to the thirty-fifth year. Even when arteriosclerosis is extensive, it is not everywhere equally marked. The lesions predominate in the small arteries, where friction is more energetic, and near the angles, curves, and divisions, where the impact of the blood current is stronger. On the other hand, however, it seems that the process is essentially regional, and that the territories chiefly affected are those which correspond to the most active parts. Comparative pathology has shown us that arteriosclerosis is frequent in animals. In the horse it is localized in the lower portion of the aorta —that is, in the vessel charged with the function of supplying blood to the most active muscles.

Arteriosclerosis, while especially marked in the radial vessels of labourers, seems to affect the arteries of the head in men addicted to mental occupations, and quite often begins in the temporals. There are evidently many exceptions to these rules, which, however, appear to be sufficiently well established to warrant citation.

An artery affected with sclerosis may be the seat of various disturbances. The disappearance of the muscular fibres from the walls of arteries lessens their resistance and often leads to dilatations, aneurisms of calibre, or miliary aneurisms. The part thus affected may burst, as is frequently the case in miliary aneurisms. In other instances the blood coagulates in contact with the diseased vessel wall, particularly when the latter has suffered atheromatous or calcareous degeneration. According to the diseased vessel, necrobiosis or gangrene will be produced. For example, in the brain a focus of softening will appear; and in the extremities, dry or senile gangrene.

Simultaneously with the appearance of arteriosclerosis, analogous changes occur in the viscera.

There has been much discussion as to the relations existing between arterial and visceral sclerosis. In this connection four principal theories have been advanced: Drs. Huchard and Weber assume the occurrence of a periarteritis radiating from the affected artery toward the neighbouring tissues. Dr. Martin believes that a nutritive disorder due to deficient circulation exists. The most differentiated—i. e., the most delicate—parts are the first to degenerate and be replaced by fibrous tissue. Ziegler goes further, and states that there is an obliteration of the small vessels. According to this third hypothesis, sclerosis would be a cicatrix of a necrosis of thrombotic origin. Finally,

according to Brault and Nicolle, scleroses of arteries and viscera are dependent upon the same causes; they are simply of simultaneous origin.

Evolution and Clinical Forms of Arteriosclerosis.—Clinically arteriosclerosis develops in such a manner that three stages may be admitted:

In the first stage the arterial phenomena predominate. This is the case in individuals who have passed the age of forty. One of the first and the most important manifestations experienced by them is dizziness. The subjects complain of dyspnœa, which is sometimes of an asthmatic character, somnolence after meals, and hemicrania. It is well to mistrust so-called asthmas and hemicranias occurring in persons of a certain age. These manifestations nearly always point to an arteriosclerosis and often announce an alteration of the kidneys. At the same time, especially in women, there are observed vasomotor disturbances, sudden congestions and sensations of heat, which are only too often charged to the menopause.

If these first phenomena be well interpreted, they lead to an examination of the circulatory apparatus. On auscultation of the heart a tympanitic click is heard accompanying the second sound, and at times even systolic and diastolic murmurs, which, however, are transient and intermittent. The arteries are somewhat hard; the sphygmograph shows a flattening at the summit of the line of ascension. The sphygmomanometer indicates an elevated pressure—20 centimetres on an average.

In the second stage the manifestations are localized—i. e., predominate in a viscus. The disturbances, however, are transitory and intermittent, and are produced only on the occasion of excessive functional activity. Professor Grasset has felicitously compared these phenomena to the *intermittent claudication* (limping) observed in old horses affected with atheroma of the lower portion of the aorta, and which occurs only at times of somewhat hard work. The muscles, sufficiently nourished when they are at rest, do not receive blood enough to enable them to continue their activity; being deficiently supplied, they contract badly. The same manifestations may be observed in man, in whom an intermittent claudication of the limbs is noted; but, according to Grasset's expression, an intermittent claudication of the organs more frequently exists. Such are transitory paroxysms of asystole, cerebral clouding, and slight accidents of uræmia with a little albumin.

The third stage is characterized by the localization of the process, or at least by its predominance in an organ. According to the part affected, four clinical types may be admitted:

Arteriosclerosis of a *cardiac type,* in which the heart, invaded by sclerosis (sclerotic myocarditis), weakens progressively. The patient falls into a state of remarkable asystole, not as a result of the intensity of the symptoms, but owing to their persistence and the impossibility of a complete disappearance of the disturbances.

Arteriosclerosis of an *arterial type,* characterized by the development of vascular dilatations, and particularly aneurisms.

Arteriosclerosis of a *cerebral type*, starting with vertigo and hemicrania and terminating in softening by obliteration of the diseased vessels, or in meningeal and cerebral hemorrhage resulting from rupture of a miliary aneurism.

Arteriosclerosis of a *renal type*, anatomically characterized by an interstitial nephritis, and clinically by polyuria, slight and often transitory albuminuria, cardiac palpitations, arterial overtension—going as high as 25 centimetres—and a galloping murmur. It ends in death by uræmia, asystole, and sometimes by pulmonary apoplexy.

Therapeutics.—It is difficult to combat the development of sclerosis. Only one medicine seems capable of arresting the advance of the process, and that is potassium iodide. In order to obtain good results, this drug must be prescribed in small and long-continued doses. It may be given in daily doses of 20 or 25 centigrammes for about three weeks, to be resumed after an interruption of ten days or so. It should be continued in this way for a year and more. Simultaneously, the circulation may be facilitated by stimulating dilatation of the vessels. To this end, three medicines are useful—namely, sodium iodide, trinitrine, and amyl nitrite. Sodium iodide acts slowly, and is to be given in doses of 1 gramme daily. The action of trinitrine is more marked and rapid. It is prescribed in doses of 1 or 2 milligrammes. Amyl nitrite, on account of its instantaneous effects, best serves against such accidents as are to be combatted immediately. The inhalation of a few drops of it evaporated from a handkerchief may ward off the various paroxysms to which arteriosclerotic subjects are exposed, such as angina pectoris, vertigo, and asthmatic dyspnœa.

CHAPTER XVII

TUMOURS

Division and classification of tumours—Embryogenetic and histogenetic tumours—Benign and malignant tumours—Typical and atypical tumours—Development of tumours—Consideration on the etiology—Relationships between inflammation and tumours—Pathogenetic theories—Parasitic theory—Therapeutics.

TUMOURS constitute an artificial group whose already well-advanced divisions will be continued and completed with the progress of science. In his justly celebrated treatise, Virchow described the lesions of tuberculosis, glanders, and syphilis along with tumours. To-day these are held by all to be of infectious origin. For a long time actinomycosis was looked upon as sarcoma, and, in fact, the microscope revealed in actinomycotic lesions a structure justifying this conception. The discovery of the pathogenic agent, however, has brought the question to its proper position. Likewise, the various sarcomatoid lesions have been referred to tuberculosis as the result of bacteriological researches. In the dog, for example, Koch's bacillus gives rise to lesions of a neoplastic character, which had long been considered as malignant tumours.

Even quite highly organized parasites may give rise to the development of tumours. With Cadiot and Gilbert, we have observed in a female dog vaginal polypi due to the presence of acarus. Albarran and Bernard had the opportunity of studying a tumour of the bladder which possessed all the characters of epithelioma, but which, in reality, was due to the eggs of *Bilharzia hæmatobia*.

A whole series of lesions of parasitic origin may at present be separated from the group of tumours; the remainder comprise productions the nature of which is absolutely unknown, but which, according to perfectly acceptable theories, seem to be referable to animate agents.

Division and Classification of Tumours.—The insufficiency of pathogenic data compels us to retain the old division of tumours into *benign* and *malignant*. This division is justified from both a clinical and pathologico-anatomical standpoint.

Benign tumours may be considered as hyperplasias of inflammatory origin; such are best exemplified by the keloid, an exuberant fibrous production developing in cicatrices. Histological examination demonstrates that benign tumours are made up of tissues having a normal arrangement, or at least preserving some of the characters recalling their origin. When adenoma is studied, it is found to have a glandular structure. The cells have proliferated and filled the alveoli, but they have preserved their general arrangement; they remain inclosed by the limiting membrane, and manifest no tendency to invade the surrounding tissues.

In malignant tumours, on the other hand, the disorder is absolute. The cells, which are of varied form and fantastic in aspect, are inclosed in alveoli of new formation; they penetrate the limiting membrane and invade the neighbouring tissues. Malignancy, therefore, is characterized histologically by irregularity of form and structure.. According to the felicitous expression of Dr. Bard, the process is one of cellular anarchy.

Embryological Tumours.—A group of productions sufficiently well defined is usually classed with the tumours. We refer to those which are due to defects of development—i. e., to embryogenetic disorders. We shall divide them into four groups: The first and second comprise those tumours starting during the embryonal or fœtal period of a being; the third and fourth consist in post-natal morbid processes occurring in the reproductive organs.

Of the embryological tumours, we may first cite the *parasitic grafts.* In studying teratology, we have seen that two spermatozoa, penetrating into one ovule, give birth to two beings, which develop side by side. In many cases, one of the two develops in a normal manner, whereas the other remains rudimentary and constitutes a more or less deformed mass, which may become inclosed in its well-constituted fellow, and thus form a tumour. Critzmann has attempted to generalize this process and offer it as an explication of the development of all neoplasms.

A second group is represented by *defects of development,* of which three types may be admitted.

Under the influence of unknown causes, a bud springing from certain parts will become inclosed in neighbouring or subjacent parts. This process is observed especially in branchial clefts, where the ectodermic and endodermic layers come into contact. An irregular union of the clefts explains the development of dermoid cysts of the neck. This is also an instance of particular evolution, which Cohnheim has attempted to generalize, by assuming that all tumours can be explained by the theory of *inclusion.*

To the second variety belong cases of *heterotopy*. An aberrant lobe of an organ may produce a tumour by anomalous development. For example, accessory suprarenal capsules may penetrate into the kidney, vegetate there, and give rise to neoplasms.

Lastly, in some cases *transitory organs,* such as the Wolffian duct and Müller's canal, persist, at least in a part of their extent, and thus give rise to a tumour.

All the productions which we have thus far studied were connected with the development of the being; those of which we are presently to speak are dependent upon *anomalies of fecundation.*

It is admitted that in certain instances tumours take their origin in the sexual glands. Facts of this kind are observed chiefly in the ovaries. Two theories are presented: one assumes an ovular fecundation, the other parthenogenesis.

According to the advocates of the first doctrine, a spermatozoon makes its way into the Fallopian tube, arrives at the ovary, and fecundates an ovule which enters upon segmentation. As it does not there find conditions favourable for its development, it gives birth to a monstrosity which constitutes a variety of *dermoid cyst.* Opposed to this theory is that of *parthenogenesis.* An ovule, stimulated perhaps by a normal concomitant or preceding fecundation, makes an abortive attempt at segmentation, which results in the production of a tumour. Although dermoid cysts are in most cases congenital tumours to be explained by inclusion, there are instances in which they seem to be developed after birth. In certain cases where the integrity of the ovary had been proved during a laparotomy, subsequent intervention has been necessitated by a dermoid cyst which did not exist at the time of the first intervention. Lastly, there remain two types of tumours dependent upon an incomplete development of the being. These tumours are observed in the uterus. One of them, known as *mole,* is produced by a myxomatous degeneration of the fœtal mesoderm. This is an innocent lesion, curable by means of simple curettage. The other behaves as a malignant tumour. This is known as *deciduoma,* which develops at the expense of the placental epithelium and of the fœtal ectoderm.

Histogenetic Tumours.—Those tumours not of embryonic origin, and which, in contradistinction from the latter, we call *histogenetic,* may be divided into four groups, according as they develop from connective, muscular, nervous, or epithelial tissue.

In each group there are to be admitted a certain number of varieties, which are very easily remembered, as each of them corresponds to a normal tissue.

The tumours of the *connective group* may be of an embryonic

nature. These are the *sarcomata,* which are remarkable for their tendency to extend. Clinicians have considered them as transitional between the benign and cancerous tumours. They are tumours with a variable prognosis.

The other connective-tissue varieties give origin to tumours whose tendency to spread will be the weaker the less vitality the tissue possesses in its normal condition. *Myxoma* corresponds to mucous tissue, *fibroma* to fibrous, and *lipoma* to adipose tissue.

The derivatives of connective tissue—i. e., cartilage and bone—give origin to *chondroma* and *osteoma.*

Vascular tissue belongs to the same blastodermic layer. We may therefore include under the same group the *sanguineous* and *lymphatic angiomata* and *endotheliomata* produced at the expense of serous membranes, representing derivatives of the lymphatic system. *Lymphoma* may also be included here.

Muscular tissue gives origin to but two species of tumours. These are *leiomyomata* and *rhabdomyomata,* which correspond to the non-striated and the striated muscle fibres respectively.

Two types of tumours may also take origin from nervous tissue—namely, *neuroma* and *glioma.* The latter has often been considered as sarcoma. This, however, is an error due to a false idea which, up to a recent date, prevailed in regard to the blastodermic origin of neuroglia. At the time when the neuroglia was held to be the connective tissue of the nervous centres—that is, a mesodermic production—the comparison was acceptable. At the present time, however, it is known that the neuroglia is an ectodermic production. Glioma, therefore, is a tumour claiming its proper place.

The most interesting facts are found in connection with tumours of epithelial origin. Passing by the *papillomata,* which are small tumours of little importance, due to an excessive development of the papillæ of the skin and mucous membranes, and which might just as well be classed among tumours of connective-tissue origin, we come to the consideration of the two great categories of *adenomata* and *epitheliomata.* Between the two we shall place *cysts,* which may be classed with one or the other group, as the case may be.

Such, in its entirety, is the classification of tumours, according to the most recent investigations and the data obtained from embryology and histology.

In order to facilitate recollection of the different types which we have here admitted, we give the following tabulated representation summarizing the general notions above referred to:

Tumours.

Embryogenetic.

Beginning during intrauterine life.

Defects of development...
$\left\{\begin{array}{l}\text{Parasitic grafts.} \\ \text{Inclusion.} \\ \text{Heterotopy.} \\ \text{Persistence of a transitory part.}\end{array}\right.$

Developing during the genital period.

Acquired dermoid cysts.   (Parthenogenesis?)

Intrauterine tumours..... $\left\{\begin{array}{l}\text{Mole.} \\ \text{Deciduoma.}\end{array}\right.$

Histogenetic.

Of connectivo-vascular origin.

Sarcoma.
Myxoma.
Fibroma.
Lipoma.
Chondroma.
Osteoma.
Hemangioma.
Lymphangioma.
Endothelioma.
Lymphoma.

Of muscular origin.

Leiomyoma.
Rhabdomyoma.

Of nervous origin.

Neuroma.
Glioma.

Of epithelial origin.

Papilloma.
Adenoma. $\left.\right\}$ Cysts.
Epithelioma.

Between adenoma, a benign tumour, and epithelioma (a malignant tumour which corresponds to what is clinically called *cancer*) there exist numerous transitions. The typical cases, however, differ considerably. In order to comprehend the distinction, let us consider any gland. We find canals limited by a membrane which is lined with an epithelial layer. In adenomata the epithelium proliferates and new glandular alveoli appear. Sometimes the excretory orifice becomes obliterated and the glandular cavity is transformed into a cyst. However, be the evolution what it may, we always find the enveloping membrane as well as the epithelium with its fundamental and typical characters.

In epithelioma, cellular proliferation is not necessarily more prominent than in adenoma. Indeed, at times this phenomenon is even

less active. The characteristic feature of a malignant tumour lies in the disposition of the cells to penetrate or break through the basement membrane and invade the surrounding parts, behaving as true parasites.

In studying certain tumours, all the transitions between adenomatous formation and epitheliomatous degeneration may be followed. In the mamma, histological sections are often highly demonstrative. At certain points the process is still circumscribed and clearly intra-canalicular; in others, on the other hand, invasion has taken place and the tumour has assumed an epitheliomatous appearance.

The former classical distinction between epithelioma and *carcinoma* is no longer admitted. Carcinoma was at one time considered to be a tumour of connective-tissue origin, but at the present time its epithelial nature is no longer a matter of doubt. Carcinoma, therefore, is an epithelioma the cells of which are inclosed in a very plentiful stroma. According to the development of the interstices, the neoplasm is soft or hard. In the former instance it is designated as *encephaloid,* and in the latter as *scirrhus.* When the elastic fibres become abundant in the interstitial tissue, the volume of the tumour may be reduced by their retraction. This is known as *atrophic scirrhus.*

Since the studies of Malassez, epitheliomata are divided into typical, metatypical, and atypical. This division is an excellent one and may be applied to all tumours.

Typical tumours present a structure recalling that of the tissue from which they develop. Thus, in the intestine, where cylindrical epithelium exists, the tumour will be an epithelioma with cylindrical cells; in the skin and buccal cavity it will be a pavement-celled epithelioma; and in the liver, a trabecular epithelioma.

When the tumour is composed of a tissue having its analogue in some portion of the economy, but not occurring at the affected point, the term *metatypical* is applied to it. Thus, for example, chondromata are met with in the testicle or the parotid gland, and epitheliomata in the maxillæ. These facts, which at first sight are so astonishing, find an explanation in embryology. The cartilaginous tumours of the parotid are due to the persistence of remains of Meckel's cartilage; those of the testicles are due to the fact that this gland was at first located in front of the vertebral column, and that at that time some cartilaginous cells of the neighbourhood were inclosed in it. Similarly, epitheliomata of the maxillary bone originate from paradental epithelial remains.

Atypical tumours are those in which cellular evolution has completely deviated from the normal type and in which the cells often assume forms and arrangements which are without analogy in the organism.

Neoplasms may be seated in any part of the organism, but they are particularly frequent in localities where several types of tissue unite—a fact which has been made use of by advocates of the inclusion theory, according to which ectopy of one tissue toward another exists.

Development of Tumours.—Tumours develop according to the same mechanism as normal tissues. The differences that have been noted are of but secondary importance. Thus, for example, anomalous karyokinetic figures are often found in epitheliomata. Instead of two amphiasters, there may be three, four, and even five; the nuclei are irregular; the cells are incompletely divided, and may acquire a colossal volume.

Too much importance, however, should not be attached to these facts, since analogous phenomena are observed whenever proliferations are very active, as, for example, under the influence of chemical irritations. The glycogenic infiltration of cells must also be referred to activity of development. In all proliferating tissues, in the embryo as well as in the adult, great quantities of glycogen are found.

The activity of proliferation and the insufficiency of blood supply explain the frequency of cellular degeneration. Sometimes the cells undergo fatty degeneration, sometimes colloid degeneration, the latter being particularly frequent in the thyroid gland, stomach, and intestines; sometimes mucous degeneration, horny transformation, and pigmentary (melanotic tumours) or calcareous infiltration occur. In other cases the central cells become necrotic and the tumour is transformed into a cyst.

Etiology.—Tumours may be observed at all ages, but their frequency and nature vary considerably at different periods of life. In the embryo tumours are dependent upon defects of development. The most frequent are angiomata, though some exceptional cases of congenital epitheliomata have been noted.

During early infancy sarcomata are observed, located chiefly in the kidneys. At puberty, exostoses are frequent. In women, at a later period, ovarian cysts belonging to the group of adenomata and epitheliomata are encountered. From the age of fourteen onward epithelioma becomes more and more common, reaching its maximum of frequency between the age of fifty and fifty-five years.

Age exercises no less influence upon the localization than upon the nature of tumours. In children they affect, in order of frequency, the eye, where melanotic sarcoma is met with, the kidney, testicles, spleen, and more rarely the other organs. In adults the portion of the body most frequently attacked is the stomach; then come the uterus,* the liver, the mamma, and the intestine, in the order named.

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* In America, according to Welch's statistics, the uterus stands first.

Among causes explaining the development of tumours, *heredity* stands first. Some authorities have admitted indirect heredity as well as direct heredity, which, according to Delbet's statistics, is observed in from 10 to 15 per cent of the cases, according to the theory of indirect heredity. Cancer is mainly observed in families of arthritics, and this accounts for its frequency in civilized races. The great number of cases occurring in certain regions, local epidemics, and the influence of water are interesting questions which are still *sub judice.* The same statement may be made in regard to alimentation, certain authorities claiming that meat, and others that vegetables, exercise an influence in etiology.

The development of a tumour is often referred by the patient to a previous *traumatism.* In spite of undoubted exaggeration, facts of this kind are too frequent to be ignored. It is certain that contusions have been the starting point of caseous sarcomata and of testicular or mammary tumours. Tumours are, perhaps, more frequently due to friction or repeated irritation. The cancer of the testicle and scrotum observed in chimney sweepers, and epithelioma of the lip in smokers, come under this group. It is well known, however, that the so-called smokers' cancer is also observed in individuals who have never made use of tobacco.

Cancer has also been seen to develop at the seat of old cautery wounds and in ectopic testes.

In certain cases chemical and not mechanical irritations intervene. According to Hoerting and Hesse, men employed in arsenical cobalt mines are often attacked with pulmonary sarcoma.

Old affections of long duration keep up a chronic irritation, which is equally apt to favour the development of tumours. Old cutaneous lesions, such as psoriasis, lupus, and extensive cicatrices, especially those consecutive to burns, have been seen to undergo epitheliomatous transformation. The same phenomenon has been observed in mucous membranes. For example, buccal psoriasis may degenerate into epithelioma; and similar transformations occur in the vagina and uterus.

In other instances cancer is developed at the seat of a lesion kept up by a foreign body. Whether the latter be of external origin or is formed within the organism, the result is the same. In the mouth, for example, a carious tooth will keep up a lingual ulceration, which, although at first simple, may subsequently become cancerous. In the stomach the exciting agent may be a foreign body which has accidentally been swallowed; and in the biliary passage hepatic calculi may be the causative agents—a fact which explains the greater frequency of cancer in the biliary passages of women, who are more often

affected with lithiasis, whereas in men cancer of the liver is mainly encountered.

Finally, lesions which were for a number of years dependent simply upon a chronic inflammation may, at a given moment, terminate in cancer. Between simple inflammations and epitheliomata there are innumerable transitions. We have already shown the frequency of hyperplastic processes in all inflammations. When the stomach is affected, as is most frequently the case, glandular alveoli develop, undergo adenomatous transformation, and the adenoma is subsequently transformed into cancer. This process is clearly observed in chronic gastritis, and still more clearly in cases of gastric ulcer.

Examples of the same order may be presented in connection with other parts of the organism. In the intestine, for example, the phenomena are developed in the same manner as in the stomach; in the liver and kidneys epitheliomatous tumours, improperly called adenomata, have often been seen to ingraft themselves upon a cirrhosis or an interstitial nephritis.

Pathogenesis.—In order to explain the development of tumours, and especially of cancer, many hypotheses have been advanced. By generalizing from a particular case, Cohnheim maintained that neoplasms are due to inclusions occurring during the embryonal period, the masses of nonemployed cells developing at a later date, as a result of a lack of resistance on the part of neighbouring tissues. A good many objections may be raised in opposition to this theory. First, it necessitates two hypotheses—namely, on the one hand, inclusion, and, on the other, feebleness of parts surrounding the invaginated elements. By admitting the reality of these two conditions, it is not readily understood why the cells remain inactive for years to become active at the moment of involution. Nor is it comprehensible why traumatism, organic lesions, and chronic inflammations serve as a starting point for the tumour. It would be necessary to maintain that fœtal inclusion has occurred precisely at that point. Finally, tumours which we know to be of embryonic origin—e. g., dermoid cysts—behave quite differently, and the cells contained in them are of adult type, advanced in development, and not active cells, as are those in neoplasms.

The same remarks are applicable to the views of Bard, who assumes the occurrence of monstrosity in the cellular development, and who thinks that the mutual induction exercised by the various cells upon each other is broken. It is evident that the reality of these various hypotheses should first be demonstrated.

In contrast to the theories of Cohnheim and Bard, who assume a disturbance of development in tissues, and dropping out of considera-

tion the theory of Rindfleisch, who explains the development of tumours by the absence of nerves, we find a more modern conception which, far from seeking the cause of the phenomena in an internal deviation, places it outside of the organism. This is the *parasitic theory of cancer.*

In favour of this theory, it may be remarked that a great number of lesions formerly considered as tumours are to-day classed with the group of parasitic affections. Without referring to tubercle, it will suffice to mention actinomycosis.

A second argument is drawn from the evolution of cancer. The cancerous cell behaves as a parasite; the lesions have an invading march and may spread in the manner of grafts. An epithelioma may propagate by contiguity from one lip to the other, and from the stomach to the liver or pancreas; it may invade the lymphatics or extend from one viscus to another through the process of embolism; it may become generalized and give rise to *miliary carcinosis,* the evolution of which recalls that of acute tuberculosis.

There are on record certain facts which tend to prove even the inoculability of cancer, and in regard to subjects suffering from cancer the fact is unquestionable. The transmission of cancer from diseased to healthy man is, however, less well established, notwithstanding a few observations in which cancer of the penis has been observed in men whose wives were affected with carcinoma of the uterus. Experimental pathology does not confirm this result. Attempts to inoculate human cancer into animals, or from one animal to another of a similar species, have thus far been wholly unsuccessful. The only positive results have been observed by Hanau and Moreau in rats and mice. According to Ménétrier, inoculation is not successful unless practised upon animals of the same family, in which cancer has already appeared, and subsequently manifests itself in several individuals of that family. This is, as it were, making the inoculation upon the subject himself. In regard to innocent tumours, the transmissibility of warts and vegetations occurring upon the genitals of man and animals is well established.

The parasitic nature of tumours is not supported by sufficient proofs to warrant acceptance of this theory. The question is simply one of persuasion. To change the theory into a certainty, it is evidently necessary to discover the pathogenic agent, and attempts thus far made have resulted negatively.

The microbes described by Rappin and Scheurlen in 1883 and 1887 respectively have quickly passed into oblivion. It may be asked whether the coccidia observed by Thomas and studied in the vegetating follicular psorospermosis by Darier, Malassez, Albarran, Foa,

and Ruffer are actually the cause of tumours. In reply to this question, it may be stated that the preparations and drawings furnished by these authors have not offered convincing evidence. On the contrary, many histologists maintain that the figures given as examples of intracellular coccidia are in reality dependent upon degenerations occurring in the cancerous cells. The discussion will last as long as the parasite eludes cultivation.

Since the contributions of Busse, San Felice, and Maffucci, attention has been directed to the blastomycetes. Yeasts have several times been found in tumours. Curtis was able to isolate and cultivate a species and also to produce tumours in animals by inoculation. Here, then, is another neoplastic production which passes into the group of parasitic lesions.

It is probable, if not certain, that division will continue, and that in the near future all tumours will be considered as due to animate agents. This, however, is only a hypothesis which is supported by a small number of facts.

Furthermore, what convinces us that the parasitic conception must be real is the fact that tumours not only propagate and become generalized, as do infectious lesions, but they produce in the entire organism modifications which can hardly be explained in the absence of this hypothesis. The rapid emaciation, special cachexia, visceral lesions, nutritive disturbances, and notably the diminution of urea (Rommelaere), seem to demonstrate the intervention of a parasitic cause. We are even naturally led to ask whether intoxication by products engendered in the tumour may not play an important rôle. Notwithstanding some positive results, it must be acknowledged that the majority of experimenters have failed to discover any toxic substance in the tissues of neoplasms.

Whatever theoretical idea may be adopted, discussion is useless. Neoplasms must be treated as parasitic lesions; they must be extirpated, and that, too, as soon as possible. Internal medication is absolutely valueless; there are no specifics or antiseptics which will oppose them. Interstitial injections, except possibly those of arsenic, have met with no better success. However, it has been observed that neoplasms, notably sarcomata, were apt to subside under the influence of an intercurrent erysipelas. Coley conceived the idea of turning this result to account in therapeutics. His method, which consists in injecting a mixture of sterilized cultures of streptococcus and *Bacillus prodigiosus,* seems to have met with some success, at least in the case of sarcomata. The procedure has been modified by Schoull, who employs the serum of animals infected with streptococcus. The results have been too discordant to lead to any definite opinion. The

same remark may be made concerning the method of Richet and Hericourt, who prepare a serum by injecting cancerous juice into animals.

In brief, all these attempts, however interesting they may be, have as yet yielded no practical results. An early and radical extirpation of the affected part and corresponding ganglia must be resorted to, and it is well to remember that, in spite of all precautions, recurrence too often supervenes at the end of a certain time.

CHAPTER XVIII

CELLULAR DEGENERATIONS

Various forms of cellular degenerations—Cloudy swelling—Granulo-albuminous and granulo-fatty degenerations—Mucoid degeneration—Hyaline and amyloid degenerations—Glassy degeneration and coagulation necrosis—Caseous degeneration—Pigmentary degeneration—General etiology and pathogenesis of degenerations—Special study of fatty, amyloid, and pigmentary degenerations.

Division and Classification.—We have repeatedly pointed out the degenerations which occur in cells. In treating of inflammation and in describing tumours we show the frequency of alterations of cellular protoplasm.

The first stage of cellular degeneration is marked by the occurrence of *cloudy swelling*. The cells are swollen and filled with an albuminous or serous fluid holding small granules in suspension. The latter occur in two forms, namely, in *granulo-albuminous degeneration*, which is the first stage, and in *granulo-fatty degeneration*, which is the second stage. In the former instance acetic acid swells the granules and then dissolves them; in the latter the granules are coloured dark by osmic acid. This morbid state is observed in a great number of inflammations; it affects the protoplasm and may attack the nucleus and nucleolus.

At a more advanced stage we find *fatty degeneration*, properly so called, or *steatosis*. This process, which plays a considerable part in pathology, must not be confounded with *fatty infiltration*, which, for instance, is observed in obesity. In fatty infiltration there is simple deposition of fat in the interior of the cell; the protoplasm may be pushed aside, but its activity is hardly disturbed. In steatosis or fatty degeneration, on the other hand, the protoplasm itself is transformed into fat. Under the influence of nutritive disorders, the proteid matter undergoes a special metamorphosis; therefore the physiological activity of the element is also profoundly affected, weakened, or even completely lost.

Mucoid or colloid degeneration is observed in the epithelial cells. It is characterized by the deposition of mucinoid substance in the

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interior of the protoplasm. This may be compared with *vacuolar degeneration,* in which vacuoles appear to be present in the cell. This phenomenon is in reality due to the presence of small cysts filled with an albuminoid matter. In colloid degeneration the material elaborated in the diseased cell may be expelled. If it enters an excretory duct it will be eliminated from the organism. Such, for example, is what takes place in the kidney: the colloid masses exuded from the cells into the lumina of the tubules unite to form *cylinders,* or so-called *casts,* which are revealed in the urine on microscopical examination. When the substance is retained at the point of elaboration, it gives rise to the development of more or less voluminous cysts. Thus are explained the *cystic degenerations* of the kidney and liver, the formation of colloid cysts in the thyroid gland, etc. The same process, however, may also affect the pathological cells—cysts may be produced in tumours. The ovarian cyst, for example, is looked upon as an adenoma or epithelioma accompanied by colloid degeneration.

Another important variety of degeneration is represented by *hyaline degeneration.* It is essentially characterized by the production of refractive homogeneous masses. It is frequently observed in certain forms of nephritis, in inflammation of the ovary, and in tuberculosis; and it is not rare in the small aneurisms which are found in the walls of tubercular cavities. According to Armanni, hyaline degeneration is frequently observed in the tubes of Henle in diabetic kidneys. The alteration found here, however, should be carefully distinguished from hyaline degeneration, for, as Ehrlich has shown, it is really due to an infiltration of the cells by glycogen.

Parallel with hyaline degeneration may be placed *transparent degeneration,* observed by Hanot and Gilbert in the livers of persons dead of cholera. In this condition the protoplasm of the hepatic cells becomes completely transparent, the nucleus alone persisting.

Finally, Zenker's *waxy degeneration* is generally considered to be the same as hyaline degeneration. It is an alteration attacking the striated muscles. It was first encountered in the myocardium in typhoid fever, and was subsequently observed in a great number of infections; it may also be experimentally produced by tetanization of the muscles. It is essentially characterized by swelling, hyaline metamorphosis, and fragmentation of the muscular tissue.

There is nothing precisely known concerning the nature of hyaline degeneration. It has been found that the substance which infiltrates the cells resists reagents. This fact has caused it to be compared to another variety of degeneration, which we shall study in a special manner—namely, *amyloid degeneration.*

Hyaline degeneration must not be confounded with *glassy degen-*

eration. The latter is essentially characterized by a transformation of the cell, all parts of which lose their histochemical properties. The protoplasm, nucleus, and nucleolus are no longer differentiated. It would seem, therefore, that this process should be identified with the one already described in the section on inflammation under the terms *fibrinoid degeneration* or *coagulation necrosis.* As we have already stated, this is a process similar to the one presiding over the coagulation of organic substances containing fibrine.

It is often stated that glassy degeneration is the first stage of *caseation.* In fact, it seems certain that the cells are first attacked by coagulation necrosis before undergoing the transformation or, one might almost say, the special fermentation which ends in their caseous degeneration. This process, which is mainly observed in tuberculosis and syphilis, has already been described in connection with the histogenesis of tubercle.

There still remains *pigmentary degeneration,* which is characterized by a transformation of the protoplasm. It should not be confounded with pigmentary infiltration, which is due to a simple accumulation of pigments transported to the cell. The difference here is the same as that between fatty degeneration and fatty infiltration.

A *sclerotic degeneration* also is often spoken of. This is the process which we have already described as a mode of repair, a veritable cicatrization. Connective tissue develops in order to replace cells that have degenerated or disappeared. The cicatrized tissue is sometimes infiltrated with calcareous salts. This process is known as *calcareous degeneration.*

Causes of Cellular Degenerations.—Although degenerations differ in their anatomical and clinical expression, and occur under conditions peculiar to each of them, and also have a dissimilar significance and evolution, the numerous varieties just described are, nevertheless, united by analogous etiological and pathogenic conditions.

Cellular degenerations always give expression to some nutritive disturbance. The latter may depend upon three distinct causes: (*a*) Deficient supply of materials destined for nutrition; (*b*) vitiation of the interstitial plasma—namely, an intoxication disturbing nutritive metabolism; and (*c*) disturbance or suppression of the functions of the cell.

Thus viewed, it is easy to conceive the etiological conditions.

At the head of the first group is naturally placed starvation. Now, it has been demonstrated by a great number of observations and experiments that suppression of alimentation is quite speedily followed by cellular degeneration. The form of degeneration produced under such circumstances is fatty metamorphosis.

The same effects are observed when the blood is altered, either because it no longer brings to the cells a sufficient amount of aliment, or because it is not charged with a requisite amount of oxygen. The former condition is realized when the blood mass is lessened—for example, as the result of great hemorrhages; the latter occurs when the blood corpuscles are altered or decreased in number, as in anæmia. At all events, the cells soon undergo fatty degeneration, the frequency and extent of the lesions varying, however, according to the type of anæmia. While steatosis is exceptional in cases of chlorosis, it is constant in pernicious anæmia.

General disturbances are not the only active factors; local anæmias play a part which is by no means unimportant. Arterial strictures and obliterations cause degeneration of those parts insufficiently supplied with blood.

It is stated that accumulation of carbonic acid in the tissues produces the same effect as an insufficient supply of oxygen, and this explains the occurrence of degeneration in cases of venous obliteration or cardio-pulmonary insufficiency. In this case, however, the process is rather one of intoxication, and we are thus led to our second group.

It may be well to consider successively the rôle of exogenous and autogenous poisons.

A very great number of mineral poisons give rise to cellular degenerations. It will suffice to mention arsenic, and especially phosphorus. The latter substance produces diffused steatosis of all the anatomical elements, its action being particularly marked in the liver, which, in grave cases, undergoes complete degeneration. It is also by the production of cellular degenerations that other substances give rise to cirrhoses. Sclerotic tissue makes its appearance to fill the vacancy created by the death of the more highly organized elements.

The degenerations and scleroses consecutive to endogenous intoxications are explained by the same mechanism. Whether the question be one of noxious products developed under the influence of cellular life or one of substances formed by bacteria normally or accidentally inhabiting our bodies, the result is the same. Let us assume, for example, that a calculus obstructs the exit of the bile. This secretion will excite a degeneration of the hepatic cells, and, passing into the circulation, will alter distant organs, particularly the kidney, in which it will give rise to a granulo-fatty degeneration of the epithelia. Let us now consider an exaggeration of gastrointestinal putrefaction. Under such circumstances a degeneration of the hepatic and renal cells will frequently be observed as the result of the absorption of the

excessive amount of toxines formed. As a dyspeptic liver exists, there is reason for describing a dyspeptic kidney. A good many cases of Bright's disease are referable to no other causation. Finally, we hardly need recall the fact that infection means intoxication, and that the soluble substances generated by the microbes produce numerous cellular degenerations. This result has been demonstrated by a large series of clinical observations and experiments. There is no subject which has been better studied. It is in the course of infectious diseases that the numerous varieties of degeneration above described are met with—namely, from cloudy swelling to steatosis, coagulation necrosis, and amyloid degeneration.

We have stated that degeneration may be due to a suppression or disturbance of cellular activity. We must here introduce an important distinction. In cases of simple lack of function degeneration occurs, and not atrophy. The muscles of an individual who remains inactive diminish simply in volume; when a limb is placed in an immovable apparatus, it atrophies but does not degenerate. The same is true of glands which remain at rest. On the other hand, degeneration is produced when lack of activity results from functional disturbance. If, for example, a muscle or a gland remains at rest because its nutrient vessels are altered, or because the nervous cells commanding the functions or the nerves transmitting the impulses are affected, it is not atrophy, but degeneration that occurs. Thus, section of a nerve does not act upon the muscle through the immobility which it causes; on the contrary, the phenomena are more complex; there is a suppression of the necessary stimulus, and degeneration seems again to be connected with a trophic disorder.

Without wishing to even briefly study the different varieties of degenerations, it may be well to give some complementary information concerning those most often met with and which have thus far only been alluded to—i. e., fatty degeneration and amyloid degeneration. We will then present some considerations relative to pigmentary degeneration.

Fatty Degeneration.—*Fatty degeneration* or *steatosis* is essentially characterized by a fatty transformation of the nitrogenous matter which enters into the constitution of anatomical elements. As already stated, it should be carefully distinguished from *fatty infiltration*, which is in reality *cellular obesity*. A provision of fat is made in the cellular membrane, and, in order to make room for it, the protoplasm is slightly pushed aside. There is an addition of a new substance, and not metamorphosis of one already existing. From this point of view, the analyses of Perls are highly demonstrative. In fatty infiltration, the water contained in the tissues disappears and gives place to the fat;

in fatty degeneration, on the other hand, the albuminoid constituent yields its place to the fat element.

Fatty degeneration may be established at once or follow another variety, such as granular degeneration, cloudy swelling, or albuminous infiltration. Under the microscope, in specimens fixed by means of osmic acid, fat appears in the form of small black coloured granules, isolated or united in masses, and particularly abundant around the nucleus. This steatosis is frequent in the liver, kidney, myocardium, and muscles. It originates under the most varied conditions. Nutritive disturbances produced by high temperatures are considered important causative factors. The frequency of steatosis in infections is thus explained. It is well to note, however, that in this instance the problem is a very complicated one, since the alterations may more easily be accounted for by a production of toxines than by thermal elevation. Nevertheless, the intervention of the latter pathogenic condition may be accepted, because fatty degeneration has been produced experimentally in animals whose temperature was mechanically raised by prolonged confinement in an oven. The alteration is supposed to be due to a lack of oxidation, since, under the influence of hyperpyrexia, the red blood corpuscles take up less oxygen than normally.

The steatosis occurring in grave anæmias, particularly that observed in progressive pernicious anæmia, has likewise been referred to a lack of oxidation.

The same influence may be applied to other etiological conditions. The steatosis manifesting itself in the course of fevers, cachexias, and poisonings may always be explained by deficient oxidation.

Finally, steatosis is observed when an organ is rendered inactive in consequence of suppression of nervous excitation, because metabolism does not progress in a normal manner. Nervous influence is indispensable for the regular performance of nutrition. If nutrition fails, oxidation diminishes and fatty degeneration is produced. The more active an organ is, the greater are its demands for oxygen. Consequently, if the supply of this gas be diminished, degeneration will affect first those parts which manifest the greatest physiological activity. Among the muscles, the myocardium is first attacked, then the diaphragm; among the glands, the liver and the kidneys.

It is well to note that steatosis occurs when there is diminution but not suppression of oxidations. Stricture of an artery produces fatty degeneration; its obliteration, if not partially compensated by collateral circulation, results in necrosis. Suppression of oxidation ends in the death of the cellular element.

The effects of steatosis may vary according to the organ attacked and the extent of the lesions. It is therefore not practicable to give

a general description of the process. In order to fix the ideas, let us consider only what takes place in the liver.

Fatty degeneration of the liver occurs in a great number of cirrhoses. Although the distribution of connective tissue serves as the basis for anatomical classifications, and to a certain extent rules symptomatology, the condition of the cell accounts for the evolution of the process. Atrophic cirrhosis is essentially a chronic affection. Hanot has described a variety which runs a rapid course, and causes death within four or five months. In this instance cellular alteration is profound and widely diffused; hence, the disease is called fatty atrophic cirrhosis. Likewise, the gravity of the fatty hypertrophic cirrhosis of Hutinel and Sabourin is due to cellular degeneration, which suppresses the function of the liver, and hence the process has sometimes been designated subacute icterus gravis.

Although rapid, the evolution lasts for months in the examples just related. Such is no longer the case when a pathogenic cause induces an acute steatosis of the cells. The affection then runs its course in a few weeks, a few days, or even a few hours. This is what takes place in the process designated by the French as icterus gravis, and by the Germans as acute yellow atrophy of the liver. It is not a definite disease. As is well known, icterus gravis may occur in the most varied conditions and depend upon the most diverse causes (see page 203). Furthermore, an infectious or primary icterus gravis, a toxic icterus gravis, and a secondary icterus gravis occurring as a sequel of various affections of the liver, have been described. The classification of these dissimilar affections under one head is permissible by virtue of the fact that the same lesion—namely, diffuse steatosis of the hepatic cells—exists in all of these morbid states. This lesion explains the symptoms. There is hepatic insufficiency, and the suppression of the functions of the liver, notably of its action on poisons, accounts for all the phenomena.

The importance of fatty degeneration may be seen from these examples. It would be easy to repeat with respect to the various viscera what we have just stated concerning the liver.

Amyloid Degeneration.—*Amyloid degeneration* was described by Rokitansky (1842) under the name *lardaceous degeneration,* by Christensen (1844) under the name *waxy degeneration,* and by Virchow (1853), who gave to it the name it now bears. In 1858 and 1859, Kekule and Schmidt showed that amyloid matter is not, as might be supposed, an amylaceous substance. On the contrary, it is an albuminoid—i. e., a nitrogenous substance.

In whatever locality it may be found, it is recognised by means of certain very simple reactions. Under the influence of the iodo-iodide

test it gives a mahogany-red colour, which becomes violet red by the addition of sulphuric acid. On contact with methyl violet it becomes red.

Amyloid matter is perhaps normally met with in certain parts of the organism. It often constitutes an epiphenomenon in the course of the most varied affections, notably of nephrites. In certain cases it may be so widely distributed that amyloidism represents the principal manifestation.

In the prostate gland and central nervous system of normal individuals there have been noted concentric masses giving a mahogany-red reaction with the iodo-iodide reagent. It may be asked, Was amyloid matter really present? Is it not more probable that these masses are simply collections of glycogenic matter? In answer thereto, it may be stated that the latter opinion prevails at the present time.

As an epiphenomenon, amyloid matter occurs in blood extravasations and in cicatrices. It is especially frequent in the kidney during the course of various lesions affecting this organ and of different varieties of nephritis, and even in acute nephrites.

In all these instances amyloid degeneration is not widely distributed; it has no clinical importance. Such is not the case with the facts which we will presently consider.

Cohnheim has related cases where amyloid degeneration had invaded the organism without any cause being revealed to account for this alteration. Such an event is exceptional. Amyloid degeneration is nearly always secondary to diseases which are liable to induce cachectic conditions, such as tuberculosis, syphilis, and multiple suppurations.

Tuberculosis stands at the head of the list. Amyloidism is chiefly observed in patients suffering with pulmonary cavities, extensive lesions of the intestine, articular or osseous suppurations, necrosis, and caries. The foci almost always communicate with the exterior.

Next comes syphilis, particularly hereditary syphilis, especially when the osseous system is involved. The spleen is the organ chiefly affected.

Suppurations of long standing may give rise to amyloid degeneration. Sometimes arthropathies or osseous suppurations, sometimes visceral abscesses, dilatation of the bronchi, or multiple abscesses of the skin are the causative factors. Finally, of the rarer causes, we may mention cancer, especially ulcerated cancer, gout, rickets, alcoholism, and malaria.

This etiological multiplicity makes it plain that all ages may be attacked. However, amyloidism is especially frequent in men and at the middle period of life—i. e., between twenty and thirty years.

Animals are not exempt from this degeneration. As in man, it is encountered in tuberculosis and in chronic suppurations. Krakow has succeeded in producing it experimentally. It is constantly observed in tuberculous pheasants, in the livers of which the tubercles are surrounded by a ring of connective tissue infiltrated with amyloid matter.

It is to-day almost universally agreed that amyloid matter should be classed as of nitrogenous origin; but the mechanism presiding over its formation is as yet unknown. Wagner considers amyloid matter as intermediate between albumins and fats; and this view would explain the frequent coexistence of amyloid and fatty degenerations. Von Recklinghausen believes a homogeneous matter is exuded from the cells, which coagulates on contact with the interstitial fluids. According to Ziegler, the diseased cells are unable to utilize the albumins escaping from the vessels, under which circumstances the albumins undergo a special metamorphosis.

It is certain, however, that amyloid degeneration is decidedly analogous to fatty degeneration, for it is produced under the same conditions, and must therefore be considered as connected with a disturbance of albuminous nutrition. No further precision can be given to this somewhat vague formula.

Amyloid degeneration affects the vessels and the connective tissue in a predominant if not an exclusive manner.

In the arteries it begins in the inner coat, sparing the endothelium. It is especially marked in the middle coat. It extends to the capillaries, which it transforms into vitreous, homogeneous tubes lined with endothelial cells, which remain intact.

When it affects the organs, it presents three different macroscopic aspects.

The totality of the greatest part of the organ is invaded; the tissue becomes homogeneous, semitransparent, lardaceous. At other times the process is limited to small foci having the appearance of sago grains.

Finally, the lesions may be minute and recognisable only under the microscope or by transmitted light on thin sections treated with the usual reagents.

The liver, which is the organ most frequently attacked, acquires a considerable volume. It becomes pasty, lardaceous, as if bloodless. Under the microscope, infiltration of the capillaries, hepatic artery, and, more rarely, of the portal vein is found. As to the changes in the cells themselves, discussion is still open. Some authors assert that degeneration occurs, others state that the vitreous masses encountered are not altered cells, but amyloid masses that have exuded from the vessels.

The localization is analogous in the other organs. In the spleen it is deposited in the Malpighian corpuscles; in the kidney it is found in the vessels, glomeruli, connective tissue, and the walls of the uriniferous tubules. The epithelial cells are frequently altered, but never amyloid. We may also mention the amyloid degeneration occurring in the lymphatic glands, the intestinal mucous membrane, and in the heart, where the muscle cells may be affected (Letulle and Nicolle).

When amyloid degeneration is localized it does not give rise to any special symptoms. Thus, in parenchymatous nephritis, where it is almost constant, it is not expressed by any appreciable manifestation.

When it is extensive it produces a certain number of phenomena, which vary according to its predominance in this or that organ. The first indications are paleness of the patient—i. e., paleness of the integuments and mucous membranes and loss of strength.

Examination of the abdomen reveals considerable hypertrophy of the liver and spleen; diarrhœa is very frequent; the urine is remarkable for its abundance, pale colour, and the great amount of albumin which it contains, at least in certain cases.

Though a fatal termination is the rule, it is, however, admitted that recovery is possible. The patient overcomes the cause that has produced the degeneration, and the latter subsides and finally disappears. Cohnheim, who has laid stress on this evolution, cites the following experiment: Fragments of amyloid matter, when introduced into the peritoneal cavity of an animal, are rapidly absorbed. Therefore, according to him, it must be concluded that absorption of this material may occur in the human organism.

This experiment is interesting, since amyloid matter is very resistant. It is not altered when submitted to artificial digestion with pepsine and hydrochloric acid. In fact, these are the means generally employed for its preparation.

Pigmentary Degeneration.—A distinction analogous to what has been admitted in regard to fat must also be made for the pigments. Sometimes there is simple infiltration, sometimes degeneration. The cells may be charged with colouring matters, particularly the leucocytes, which are often overloaded with carbon even under normal conditions. In other cases the cells may be infiltrated by more or less modified blood pigment derived from former hemorrhage. Lastly, various black pigments, apparently derived from the blood, may also accumulate in certain anatomical elements without disturbing their function.

In the case of pigmentary degeneration, on the contrary, cellular alterations are found which account for the disorders observed during life.

Pigmentary degeneration is essentially characterized by the accumulation within the cells of an okra matter (*pigment ocre* of Kelsch and Kiener, *rubigine* of Auscher and Lapicque), which has the property of turning black under the action of ammonium sulphydrate, or blue on addition of potassium ferrocyanide and dilute hydrochloric acid. The latter reaction, which is very sensitive, is employed in histology. In preparations thus treated it may be seen that the pigment invades the protoplasm, pushes it aside, atrophies the nucleus, and causes its disappearance.

All organs are not equally attacked. As is always the case, the frequency of the lesions is in proportion to functional activity. The liver is the organ most frequently invaded; next comes the kidney, then the myocardium and the pancreas.

Pigmentary degeneration is chiefly observed in malaria, then in diabetes. It is much more rarely met with in pernicious anæmia, profound anæmias, and certain poisonings. It is a serious process, which, by virtue of the special cachexia it induces, may be placed parallel with amyloid degeneration.

CHAPTER XIX

FUNCTIONAL SYNERGIES AND MORBID SYMPATHIES

Unity of the organism in its physiological state: functional synergies—Unity of
the organism under pathological conditions: morbid sympathies—Study of
functional synergies: anatomical unity and physiological unity—The contiguity of organs—Vascular connections: emboli—Nervous connections—Conclusion concerning the mechanism of general reactions and of fever.

LIVING organisms are constructed in such a manner that all modification occurring at one point of the economy influences the entire economy.

This law is equally true in physiology and in pathology.

Let us suppose, for example, that a muscular group contracts. Circulation becomes at that point more energetic, and occasions consequently an increase of cardiac activity. But, in contracting, muscles consume carbohydrates, and when their reserve is exhausted the liver undertakes to furnish them with the useful materials; here is another organ entering upon activity. Respiration will accelerate, since it must cause a greater amount of oxygen to arrive and throw out the excess of carbonic acid proceeding from the transformation of carbohydrates. Other wastes will be eliminated through the urine, and that will increase the activity of the kidney. Then, should contraction be somewhat prolonged, bodily temperature will tend to rise, and the various apparatus concerned in the regulation of thermogenesis will soon be called into play; there will follow vasomotor modifications and changes in the secretions, notably in the sweat. Finally, general nutrition being also stimulated, the result will be a loss of ternary and nitrogenous matters, and a tendency to reparation, as expressed by hunger and thirst, and consequently a general increase in functional activity.

Reciprocally, if an organ languishes, if its activity diminishes, the result is a series of reverse modifications in the entire economy—viz., a diminution in all the vital manifestations.

Along with the relations which exist between the various parts of the organism and which constitute what is called in physiology *func-*

tional synergies, we find, in pathology, *morbid sympathies* or *synergies*. The disturbances may at first be local; on a superficial examination, they seem to be limited to a part of the organism. In reality, a great number of modifications is necessarily produced in the whole economy. The reactions may be more or less marked, at times even imperceptible; they exist none the less. *There is no disease that remains local.*

We are therefore led to inquire through what mechanism the lesions of an organ influence the remainder of the economy. For convenience of description, we may group in four classes the connections uniting the various parts of the organism. These are functional synergies, contiguity of organs, vascular connections, nervous connections.

Functional Synergies

For the old idea, which assumed that each organ played a special and determined part, is substituted the more complex conception of functional synergies. We know at present that several organs collaborate in view of assuring the same function; that certain organs may supply and replace each other in a more or less perfect manner.

As the result of physiological researches and clinical observations, parts which were separated by anatomical study have been united and grouped. Physiological unity does in no wise correspond to anatomical unity; thus, for example, the motor cell, the nerve, and the muscle represent the same physiological unity, whereas anatomy distinguishes in them at least three different parts. Pathology confirms the data of physiology on this point, since the alteration of one of these parts influences the others: destruction of the cell, for instance, entails atrophy of the nerve and muscle.

In general, secondary alterations, consecutive to a primary lesion, produce an aggravation of the disease; but they realize at times a favourable modification and represent a tendency to a new adaptation. In the latter case the secondary lesions obey one of the two following laws: suppression of what has become useless; anatomical or functional modification of parts capable of compensating for the primary lesion.

These two laws are easily understood when the teachings of natural history are taken into consideration.

It is known, in fact, that function exists before the organ and represents simply a reaction to an external cause; in the evolution of beings, every change means an adjustment to new needs. If external conditions vary, reactions must be modified. New functions are thus

produced, which in time give rise to anatomical modifications, to the transformation of a pre-existing organ, or to the production of a new one. On the other hand, the organ can not maintain itself in its actual state unless the function that has given rise to its production continues to be exercised.

It is well known, for example, that the eyes of moles and of some burrowing rodents are rudimentary, or may even be completely covered with skin and hair. Several crustacea living in the subterranean caves of Carniola and Kentucky are blind. Darwin reports that in certain oceanic islands, where no carnivorous animals exist, birds are met with whose wings have become rudimentary and who are incapable of flying. In domestic ducks, the leg bones are more developed and those of the wings less voluminous than in the wild: another illustration of the law of adjustment.

If we wish to look for analogous facts in the domain of embryology or ontogeny, we see that a series of organs disappear when they have become useless. The metamorphoses of certain batrachia, the atrophy or transformation of the branchiæ, when the animal passes from aquatic to aërial life, shows us simply this adjustment of the organ to the function.

What in this way occurs in a being who evolves, or what is acquired in successive generations and transmitted by heredity, is not different, on the whole, from that which is produced in an individual when physiological unity is affected at some point.

Let us first take some very simple examples; let us consider what happens in the vertebral column. Here is a physiological unity composed of a great number of independent pieces. Now, if one of these pieces be altered, as is the case in Pott's disease, there will consecutively be produced curves of compensation that will modify the shape of the whole vertebral column, will even reverberate in more distant parts—in the pelvis and thorax. These modifications are fortunate so far as they remedy the primary lesion and adjust the organism to new conditions, but they thus create a danger, and may become a cause of cardio-pulmonary accidents or of dystocia.

Similar changes are observed consecutively to lesions of the hip, to the shortening of a member, to a defective position—that of the sciatic, for example—to some alteration of the skeleton; there develop in the healthy parts more or less marked deviations of a compensative character, which respond to the first needs, but too often become the cause of new disturbances.

The great systems, as the circulatory or the nervous, will furnish us illustrations of greater interest.

Let us consider first what takes place in the circulatory system.

In the case of a limited lesion, of ligation or obliteration of the main blood vessel of a member, a network of collaterals will develop. This result is favourable, since it permits the re-establishment of the circulation, but it sometimes creates new dangers, of which one may easily be convinced by considering the cases where the obliteration occurs in the principal vessel of a viscus. Thus, in atrophic cirrhosis, the disturbance of portal circulation, forcing the blood to pass through the channels of derivation, may be the starting point of œsophageal varices, and consequently the cause of a mortal hematemesis.

The importance of secondary lesions clearly appears in the study of cardiac malformations. Congenital stricture of the pulmonary artery occasions persistence of the foramen of Botal, sometimes of the interventricular opening of the arterial canal, and the development of bronchial arteries. These various modifications always follow the same law, equally true in pathology, in physiology, and in natural history: re-establishment of functions on new bases and new adjustment, liable to become the starting point of new accidents.

It is especially in the study of the nervous system that the history of secondary modifications abounds in interesting facts.

The simplest illustration is represented by the neuromuscular system, including the cerebral cell, the medullary cell and the cord which connects them, the nerve, and the muscle; the lesion of the cerebral or medullary nerve cells entails degeneration of the subjacent parts. Reciprocally, suppression of the muscles affects the nerve and the cells; an amputation, for instance, gives rise to atrophy of the psychomotor centres corresponding to the suppressed part. The centres atrophy, because their peripheral expansions no longer exist: they have no longer any reason for being. Munck has experimentally realized similar facts: he has shown that extirpation of the eye causes atrophy of the optic centres.

We find similar synergies when we consider the other apparatuses of the economy, such as the digestive and the genital. Extirpation of the ovaries leads to atrophy of the uterus; double castration acts similarly upon the prostate gland.

In certain cases functional synergy allies parts that seem quite distinct: such is the alliance between the liver and the kidneys. The liver prepares certain materials necessary for the urinary secretion: nitrogenous substances undergo there an ultimate transformation which reduces them to the state of urea—i. e., a crystallizable body, which readily diffuses and represents a true physiological diuretic. If the uropoietic function of the liver is disturbed, the urea will be replaced by less oxidized bodies, some of which will prove harmful to the renal epithelium and give rise to a secondary nephritis. The

hepatic lesion often leads to the passage into the general circulation of toxic substances, which the liver should have retained and transformed; or the principles of biliary secretion, salts and pigments, invade the economy; or else an excess of glucose reaches the blood. At all events, the kidney comes to the assistance of the organism and prevents intoxication; but the additional work imposed upon it may become the cause of epithelial alterations. These results, which we will study at greater length in connection with the lesions consecutive to dyscrasias, deserve to be alluded to here, since they clearly show what may be the consequences of functional synergies.

These functional synergies are much more numerous than one might at first believe. As we are speaking of the liver, we know to-day that, through its glycogenic reserve, this gland plays a great part in nutrition; it regulates the supply for all the cells which consume sugar—namely, for all the cells of the organism. But it is especially with the muscles that the liver is in continual relation. As has been remarked by Chauveau and Kaufmann, "the liver is the indirect collaborator of the muscles in the execution of movements"; when the muscle contracts, the liver pours the sugar more abundantly into the blood. It is then conceivable that disturbances of the glycogenic function should affect muscular contraction.

Finally, there also exist altogether incomprehensible synergies between various parts of the organism. Such is the relation existing between the genital apparatus on the one hand, and the pilous system, the larynx, and even the brain, on the other. It is known, for example, that the encephalon is far less developed in castrated than in entire horses. It is true that since the researches of Brown-Séquard there is a tendency to explain facts of this nature by internal secretions: the testicle or the ovaries are supposed to produce principles useful to the nutrition of these various parts of the organism. Some explain in the same manner the correlation which exists between the atrophy of the thyroid gland and myxœdema, the hypertrophy of this gland and exophthalmic goitre, the lesions of suprarenal capsules and melanodermia. The theory is very seductive, but in some regards it may still seem inadequate; at all events, if it were generalized it would account for one of the most interesting aspects of functional synergies and their consequences—morbid synergies.

Contiguity of Organs.—The lesions of one organ may affect neighbouring organs by two quite different procedures. Sometimes the action is simply mechanical: a hypertrophied viscus compresses and pushes away surrounding parts; in other cases the affection has specific characters and excites in adjacent parts special disturbances or particular reactions.

It will suffice to reflect for a moment on the anatomical dispositions of organs and their mutual relations, in order to understand the effects produced by the peculiar development of any of them. Illustrations abound; we shall recall a few: The exudation of the left pleura compressing mechanically the heart and the vessels, may occasion serious disturbances and even sudden death; thyroidal tumours crush the trachea; tumours of the uterus and ovaries push aside the intestines and the diaphragm, and disturb the play of the lungs.

Phenomena produced by compression may be grave—e. g., the syncope resulting from left pleurisy; but the disturbances often disappear with the pathogenic cause. If pleurisy be punctured, the heart resumes its situation; if the tumours of the thyroid gland, of the uterus, or of the ovary be excised, the secondary manifestations stop. However, such is not always the case. A simple mechanical disorder may entail irremediable effects: compression exercised upon excretory passages, vessels, and nerves may produce a series of highly important modifications.

Compression of the excretory duct of a gland causes stagnation of the secreted liquid. If compression be of short duration, the disturbances will cease when the obstacle is removed; but if it be somewhat prolonged, a series of modifications in the epithelia, and consecutively in the connective tissue, will appear. The obstacle may subsequently be removed, still the glandular lesion will persist and develop on its own account. The examples of this process are exceedingly numerous: we hardly need mention the cirrhosis produced by the compression of the biliary passages, the hydronephrosis, the sclerosis and atrophy of the kidney, resulting from the obliteration of the ureter, as in the case of cancer of the bladder or the uterus. Similar occurrences have been reported with reference to the salivary glands and the pancreas. We may also mention in this connection what occurs as the result of compression or stricture of the larynx and of the trachea: the lung is affected with an incurable emphysema.

Similar phenomena are observed in the blood vessels; as a rule, they are even more rapid and more serious. If compression bears on an artery, the territory supplied by it becomes ischæmic, resulting in the production of necrosis or gangrene. In case of a vein, the blood stasis engenders œdema, and subsequently sclerosis.

Compression of the nerves is expressed by sensory modifications, neuralgias, spasms, paralyses, vasomotor or trophic disturbances, at times by speedily mortal infections, best exemplified by the pneumonia consecutive to section or compression of the pneumogastric nerve.

When a compressing organ is struck with some inflammatory or

neoplastic affection, it may, at the same time that it acts mechanically, exercise a specific influence.

An inflamed tissue often occasions paralysis in subjacent parts. Stokes long ago established this fact as regards the diaphragm in cases of purulent pleurisy. Such is exactly the case when a phlegmonous angina causes paralysis of the palate. At other times, though this is more rarely the case, it is an acute pericarditis that causes the paralysis of the myocardium. What is produced in the striated muscles is equally observed in the nonstriated; such is gastrointestinal paralysis occurring in peritonitis.

Inflammatory centres may be propagated to the surrounding organs. There sometimes occurs an unexpected opening of a purulent collection into a contiguous cavity. In most cases the opening is preceded by a preliminary step—a true extension of the inflammatory process, giving rise to a thickening of the tissues, then to ulceration and perforation; the pus thus makes its way toward the exterior. The process is often favourable, since it leads to the evacuation of the morbific matter; but it may become the source of new dangers, such as the abscess of the liver that opens into the lung and thus produces a pulmonary gangrene.

Apart from microbic lesions, there are only cancerous affections that may thus be propagated by contiguity. The cancer of the stomach may cause secondary nuclei in the adjacent parts of the liver and pancreas. The cancer of the mammary and lymphatic glands may invade the skin, etc. In most cases, however, the propagation of cancerous lesions is not effected in that way; the neoplastic cells, like pathogenic microbes, strongly tend to take the vascular (sanguineous or lymphatic) route, and to give rise in this way to foci more or less distant from the primary lesion.

One might believe, in some cases, that sclerotic lesions have extended in the same manner; sclerosis of the liver and lung have been seen to follow perihepatites and pleurisies. But the process is far more complex: the visceral lesions are due, in cases of this kind, either to the direct action of the morbific cause, which acts both on the serous membrane and on the subjacent organ, or to the compression of the nourishing vessels which supply the viscus; the consequent anæmia, by disturbing the nutrition of the noble element, brings about the compensating development of connective tissue.

Vascular Connections

Cardiac Insufficiency.—Functional disturbances and lesions of the heart, leading to modification of the circulation of the blood, necessarily affect the entire organism.

Vascular lesions, even those which seem to be best compensated, are attended by a certain number of vascular disturbances, and consequently by nutritive disorders. Examination of the facies in a person suffering with aortic or mitral lesion suffices to demonstrate the influence of the heart over distant parts. The dystrophic influence of cardiopathies is especially marked when the lesion has begun in childhood; it may be expressed by infantilism, as is at times observed as the result of aortic insufficiency. A better-known example is furnished by the history of simple mitral stenosis, giving the women affected with it a chlorotic appearance.

However, where the pathogenic influence of circulatory disturbances appears most clearly is in cases of cardiac insufficiency or asystole.

This process is essentially characterized, from an anatomical and clinical point of view, by a weakening of the myocardium and insufficiency of the tricuspid valve; from the standpoint of pathological physiology, by a diminution in the arterial and an increase in the venous tension. The result is a stasis in the organs, the liver, kidneys, and brain. If then treatment intervenes, if digitalis is administered, the contractile energy of the myocardium increases, and all the symptoms disappear; the arterial tension returns to its normal condition; the liver, which had increased in volume, diminishes; the kidney no longer permits the escape of the albumin; the urine returns to its normal quantity; the œdemas disappear. The patient believes himself re-established and resumes his occupation, but after a certain period of time a second attack of asystole occurs, then a third, then a fourth. Finally, there comes a moment when no good result can be obtained from the administration of digitalis; the congestion of the organs admits of no relief, the liver remains hypertrophic, the kidneys continue to pass out albumin, the œdemas persist. What has happened?

In the former case, when all disappeared under the influence of cardiac medication, the question was of an individual in whom the functional modifications of the organs were under the influence of cardiac insufficiency; it was therefore sufficient to increase the energy of the myocardium by means of digitalis, caffeine, or sparteine to see the accidents vanish. But when the morbid manifestations were repeated, they at length disturbed the function of the organs; the visceral congestions were followed by more profound alterations; the cells degenerated, and secondary scleroses were produced. Asystole has yielded to *cardiac cachexia*. Let us suppose that it was possible to replace the diseased heart by a normal one; the symptoms would continue none the less, because the primary disturbances of

the circulation have created, secondarily, organic lesions which evolve on their own account; the cardiac has become a pulmonary, a cerebral, a hepatic, or a renal patient. In many instances the secondary lesions are so predominant that the clinician is at a loss to trace the succession of the phenomena; in vain he endeavours to determine what has been the *primum movens* of the morbid series.

Are these secondary accidents to be attributed to the venous stasis resulting from the cardiac insufficiency, and can they be accounted for merely by hydraulic modifications? If such were the case, the viscera would have been altered according to a determined order; the inferior cava system, which empties itself with more difficulty than the superior, would first be affected, and among the viscera that are annexed the liver would be the first to receive the blood reflux from the right auricle; it would, then, be affected before the kidneys, whereas the brain would be reached after the abdominal organs. Clinical experience shows that such is the case with children; in childhood visceral asystole begins with the liver, and albuminous urine is scarcely ever observed without hepatic hypertrophy. But such is not the course of events in adults. The reason of this divergence is easily comprehended. In the child the organs are healthy; they have not been altered by the numerous infectious or toxic agents which in the adult have left in the viscera traces of their passage. Previous diseases create local susceptibilities, particular vulnerabilities; hence, in presence of the same morbific cause, each organ suffers on its own account, with the result that more mutability of symptoms, more unexpected morbid reactions, and more variability in clinical types are observed. This is the reason why visceral lesions consecutive to cardiopathies do not follow, in the adult, the regular course observed in the child; that is why we meet with pulmonary, hepatic, renal, or cerebral partial asystoles. If we were able to know exactly the past of our patients, if we could find out what defects they have inherited, if we could succeed in determining what organs had been touched and to what degree altered, we would be in a position to predict assuredly what are to be the localizations of cardiac insufficiency.

We have hitherto supposed the cardiac lesion to be primary; but such is not always the case. Through the vessels terminating in or starting from it, the heart finds itself in communication with all the parts of the organism, and therefore it is readily influenced by them.

If any disturbance is produced in the intrapulmonary circulation, as it occurs in bronchial dilatation and in pulmonary sclerosis or emphysema, the right heart, compelled to do some additional work,

will in the end dilate, and tricuspid insufficiency and the phenomena of asystole will follow. The same result is observed in tuberculosis, or, at least, in one of its forms known as fibrous phthisis; in this case emphysema and bronchiectasis exist, and it is to these various lesions that the cardiac disturbances must be attributed.

Asystole of pulmonary origin often presents, clinically, some particular characters: the pulse may be strong, regular, and arterial tension sufficiently high; there is then an evident discordance between the state of arterial circulation and the symptoms observed. The reason is that the hepatic hypertrophy, albuminuria, œdema of the lower extremities, depend upon the disorders of the right ventricle, and, in fact, it is the latter that is primarily affected, while the left ventricle continues to contract with sufficient energy. There is discord between the condition of the two halves of the heart. This fact explains why so little result is obtained from treatment with digitalis, which influences especially the left heart.

Organs other than the lung may influence the heart and bring about through it a series of new disturbances; this is observed in the kidney and the liver. We see, for example, Brightics present cardiac disturbances as initial phenomena; others succumb to asystole.

Part played by Peripheral Blood Vessels

Outside of the heart, peripheral blood vessels establish numerous connections between the various parts of the organism, and explain a great number of secondary disturbances.

Organs may be brought into relation by a particular blood system. Such is the case with the portal vein. It is conceivable, when the anatomical disposition is taken into account, that alterations affecting the spleen, the stomach, the intestine, may disturb the circulation of the liver. In most cases the reverse takes place—a hepatic cirrhosis causes congestion of the digestive canal, hypertrophy of the spleen, development of a collateral circulation, and production of ascites.

In other instances, by far more numerous, the secondary disturbances result from the compression exercised on the vessels of an organ by the parts with which the latter are in relation.

The effects evidently vary according as the compression is exercised on the afferent vessels (artery or portal system) or on the efferent (veins or lymphatic vessels). In the former case there is ischæmia or complete anæmia, in the latter a venous or lymphatic stasis. In consequence of this first stage, circulatory modifications may supervene, tending to re-establish the blood course and thus

remedying the first accidents. Otherwise, the compression will cause modifications of a trophic order: sometimes dystrophy will attack the vessel itself and produce hemorrhage; sometimes persistent ischæmia will terminate in necrobiosis and softening; finally, in other instances, venous or lympatic stasis will engender sclerosis. But in the last case we must, perhaps, as we have done with regard to cardiac insufficiency, assume the intervention of some superadded element—i. e., microbes or their toxines. Sclerosis would then depend upon an infection sufficiently attenuated not to give rise to any appreciable manifestations.

Such is not always the case; vascular disturbances often favour the development of serious infections. They play an important part in the pathogeny of diffused phlegmons, of dry or moist gangrenes; they constantly intervene in the localization of even specific processes: such is caseous pneumonia in those cases where the pulmonary artery is narrowed and compressed by a tumour or aneurism of the aorta.

In this manner, any lesion whatever which compresses the vessels of an organ produces a series of consecutive modifications, which may be summed up as follows: initial disturbances of circulation, anæmia or passive congestion, more or less complete re-establishment of circulation, sometimes development of collateral networks, or consecutive trophic disorders, necrobiosis, softening, sclerosis, and possibly pyogenic, gangrenous, or tuberculous secondary infections.

The circulatory system plays also an important part in the propagation and diffusion of morbid processes, serving as a vehicle for soluble products or foreign bodies springing from a primary focus.

We shall not dwell upon the diffusion of soluble products, of which we have already repeatedly spoken. We have shown that every cell constantly modifies the chemical constitution of the blood and thus influences the remainder of the economy. Each living element acts by seizing upon the substances necessary to its nutrition, by abandoning products of disassimilation, by secreting substances which contribute to the regulation of nutrition, finally (at least in certain cases), by neutralizing toxines and throwing them out or by producing antitoxic substances. All these products, favourable or unfavourable, are poured into the circulation and by means of vascular connections are carried to the various parts of the economy. They act on the first organ with which they come into contact. Thus, toxines proceeding from the digestive canal meet with the liver and occasion in this gland congestion and sclerosis. But the arrest is not complete; a certain quantity crosses the first barrier and diffuses into the economy. Now there are certain organs better situated than

others for mutual influence; such is the case with the liver and kidneys. The toxines originating from the liver easily go to alter the renal filter, as was demonstrated by the researches of Gouget; reciprocally, the diseased kidney affects the liver, as was shown by Hanot and Gaume. Finally, recent researches have established the fact that the lesions of the lung rapidly produce secondary alterations in the liver. It would be easy to multiply the examples. Let us keep well in mind that through the circulatory system soluble substances are transported to the whole organism, but that they do not act equally upon all the parts. Their action is particularly manifest on the organs which are found in direct relation through the vessels, and on certain cells belonging to different organs but allied to each other by virtue of functional synergies.

Besides the soluble products, the circulatory system may carry solid bodies, which go on unobstructed until the moment when, meeting with too narrow a vessel, they are forced to stop at once. To this process has been given the name embolism; its importance leads us to describe it somewhat in detail.

Embolism.—To Van Swieten is due the merit of having discovered embolism and made of it a complete study, both clinical and experimental. But men were not prepared for the new conception, and the labours of Van Swieten remained unnoticed or fell into oblivion; the discovery had arrived too soon.

In the following century, when Virchow published his works on embolism (1845–'56), physicians, prepared therefor by some researches of Magendie, Gaspard, d'Arcet, and Cruveilhier, accepted with enthusiasm the ideas of the celebrated anatomico-pathologist. The question was taken up at the right moment; it led to a series of investigations which secured a rapid progress for its study.

Embolism is generally defined as sudden occlusion of a vessel by a foreign body travelling in the circulatory system. The meaning of the word has of late been modified; some have described under the same name incomplete obliterations, and others have spoken of microbic emboli, or of foreign bodies, extremely small, unable even to obstruct a capillary. The latter stop by virtue of a molecular adhesion which retains them, as are retained microbes in a porcelain filter whose pores are larger than they.

We are thus conducted to the following definition: Embolism is essentially characterized by the sudden arrest of a foreign body carried by the sanguineous or lymphatic circulation.

Emboli are divided, according to their volume, into emboli of large and small calibre and into capillary emboli; according to their point of departure, into exogenous and endogenous emboli. The former pro-

ceed from the exterior, the latter originate within the economy. Finally, in view of their nature, they are divided into mechanical or inanimate and parasitic or living emboli.

It is now easy to take into account the various divisions of the general classification. We are thus led to group emboli as follows:

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EMBOLI

</div>

Inanimate.	Living.
Of intravascular origin.	Animal.
Cardio-vascular.	Vegetable.
⎧ Clot.	Microbic.
Sanguineous ⎨ Globules.	Cancerous.
⎩ Colouring matters.	
Of extravascular origin.	
Solid.	
Fatty.	
Cellular.	
Gaseous.	

INANIMATE EMBOLI do not act, in most cases, except in a mechanical way. They may be engendered in the walls of the heart or of blood vessels. Small vegetations emanating from an endocarditis, fragments of columns or of valves, atheromatous productions occupying the coats of large vessels, fall into their interior and are carried by the blood current.

The second group is represented by blood clots detached from the inner surface of the heart or of blood vessels, where they had been deposited under various pathological conditions. In endocarditis, arteritis, and notably aortitis, cruoric or fibrinous clots, frequently lining the altered wall, may at a given moment engender emboli. The same process is quite often observed with the aged in the auricle.

More frequently the difficulty is with a vein; its walls, invaded by a microbe, are inflamed, become rugged, and lead to the formation of a clot. The blood, stagnating behind this obstacle, coagulates in its turn, and engenders a secondary soft clot, the so-called elongated clot, which will extend to the point where the vein joins a main trunk. It will extend even beyond the junction, penetrating into the lumina of the vessel; in this way it forms a projection compared to the head of a nail, which, constantly beaten by the blood current, will easily be detached. In other cases there is an adhesion of one of the primary or secondary clots, which is not sufficiently firm, and often, at the time when the patient is about to recover, when he moves and begins to rise, the clot breaks up. More or less voluminous fragments are detached and, being thrown into the circulation, give rise to embolism.

Other varieties of emboli may be produced in the blood. Altered

red blood corpuscles represent veritable foreign bodies that will go to plug capillaries and occasion in the organs the most varied lesions. This is observed in cases of poisoning by oxide or sulphide of carbon, chlorate of potash, or chloroform. If the destroyed corpuscles are somewhat numerous, extended lesions are produced in certain viscera. In this way are explained the small centres of cerebral softening which occur quite frequently in intoxication by carbonic oxide.

Globular emboli are produced also in extensive burns and frost-bites, and explain certain phenomena. In the focus, the red corpuscles are altered, destroyed; when carried by the blood current, they produce embolism. Their action is completed by the hematoblasts which contribute to the formation of venous thromboses, followed secondarily by visceral emboli.

Matters derived from the red corpuscles may form emboli, as occurs, at least, in cases of malaria. Without admitting, with Frerichs, that the genesis of the pernicious manifestations is due to pigmentary emboli, we must recognise that the pigment emanating from the spleen and from the marrow of bones may induce various alterations in other organs.

Inanimate emboli, engendered outside of blood vessels, are represented, first, by solid foreign bodies; this variety has but an experimental interest. In order to study the mechanism of emboli, experimenters have repeatedly injected into the vessels little balls of wax and inert powders, especially lycopodium powder. An interesting group is represented by the cellular emboli that originate within the economy; they are due to the penetration of dead cells or even tissue fragments into the vessels. This is particularly observed as the result of great traumatisms. In cases of hepatic contusion particles of the wounded gland were seen to be carried to the heart and pulmonary artery. Similar phenomena have occurred in cases of puerperal eclampsia and have been explained by the existence of a hemorrhagic hepatitis. Ruge has called attention to the emboli of cerebral matter which may occur in the lungs of the newborn, when the head has been strongly compressed by the forceps, especially in cases of narrow pelvis.

In general, simply the contents of the cells, especially the fat, are thrown into the circulation.

In this manner, according to Virchow, are produced, during confinement, *fatty emboli* in the kidney and lungs; they are supposed to be due to contusions of the cellular tissue of the abdomen and vagina. At times the fat starts from an organ that has undergone fatty degeneration—from the liver, for example—and gets fixed in a branch of the pulmonary artery or in the kidney. Fatty emboli are

particularly frequent in the lesions of the osseous system. They are produced in all fractures, according to Scriba. More frequently, they originate from osteomyelitis. Of slight gravity when they are not abundant, they may, when repeated, produce pulmonary accidents and sometimes entail speedy death.

Fatty emboli have been observed also in diabetes, but their mechanism is not understood; according to Hamilton and Saunders, acetonæmic coma is to be attributed to them.

Gaseous emboli are nearly always exogenous. They have sometimes been produced by the surgeon during a transfusion or an intravenous injection. If the amount of air introduced is not too considerable, there results no harm whatever; if the air enters suddenly and in great quantity, the patient succumbs within a few minutes. Similar accidents have occurred when, in the course of an operation, one of the jugular veins is cut and, being maintained gaping by the cervical aponeuroses, suffers the effects of thoracic aspiration: the air enters into it with a special hissing sound. The same phenomenon has been observed in the uterus in cases of placent prævia: the air penetrates through the gaping sinuses.

In some exceptional cases gaseous embolus has been endogenous. Jurgensen has seen, in the course of a round ulcer, gas penetrating the vessels; he was able, during life, to recognise its presence in the left temporal and the external jugular.

ANIMATE EMBOLI represent a group still more important than the one we have first studied. They explain the propagation of animal parasites, such as hydatid, strongylus, filaria, or *Distoma hepaticum.* In cases of hydatid the embryo passes from the digestive canal into a branch of the portal vein, and it is by a true embolic process that it will go to fix itself in the liver.

The rôle of embolism in the evolution of lesions produced by vegetable parasites is not less notable.

Let us take, for example, actinomycosis: the primary focus may give rise to secondary, sometimes multiple lesions, which in some cases are sufficiently numerous to make us think of pyæmia. The same is true of cases of aphtha, and this result is comprehensible, since Wagner has shown that the oidium sends out projections into the vessels of the mucous membrane. In this way is explained the formation of visceral foci, as such examples have been recorded by Zenker and Ribbert.

But it is especially in the generalization of infectious lesions that embolism intervenes. If we can no longer admit, with Toussaint, that microbes cause death by plugging the capillaries, it is certain that they often produce, by this mechanism, secondary foci. This is what

takes place in cases of pyæmia. Starting from a primary lesion, pathogenic agents are capable of penetrating directly into the blood; in most cases they first give rise to phlebitis, whose importance in the dissemination of lesions and the production of purulent infection was noticed by old observers. The clot which microbes have colonized breaks up and its particles are thrown into the circulation. Microscopic emboli are produced which do not act only in a mechanical manner; they carry living germs which give rise to the development of secondary foci; the latter present the same character as the primary focus.

In certain instances, when the secondary lesion communicates with the external air, germs proceeding from the exterior may ultimately be introduced and transform the purulent into a gangrenous focus. This sometimes occurs in the lung.

Many other infections are propagated by the same mechanism. Such is the case with glanders and, particularly, tuberculosis. In the acute miliary forms, generalization is often consecutive to an old caseous focus; at that point is produced a specific phlebitis which permits the dissemination of the germs.

By the same process cancer is propagated. Whether this disease be, or not, parasitic, it is certain that the neoplastic cells behave exactly as parasites. They penetrate the more easily into the vessels, as they possess, when young, amœboid movements (Waldeyer). The study of the secondary cancer of the liver permits us to understand this process and to follow the evolution of the cells arrested in the capillaries of the organ; as it has been well demonstrated by Hanot and Gilbert, it is the wall of the capillaries that forms the stroma of the neoplasm. The same mechanism may be applied to other secondary cancers, notably to those of the lung. We could easily multiply the examples; they establish that the secondary foci, through the cells which they contain, repeat the primary focus, and, by their structure, recall the anatomical character of the organ in which they are developed.

Course of Emboli.—Whatever their nature, emboli follow a route traced in advance and governed by the laws of the circulatory mechanics. From this point of view they may be divided into three groups: arterial emboli, pulmonary emboli, and emboli of the portal system.

Arterial emboli start from some lesion of the pulmonary veins, of the left heart, of the aorta or one of the vessels emanating from it. If, as is most frequently the case, they are born before the aorta or at its origin, they pass generally into the left common carotid, whose direction continues that of the arch; they stop in the Sylvian

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and produce right hemiplegia with aphasia. This takes place in half of the cases.

In other instances, continuing its route in the aortic trunk, the embolus is arrested in the splenic, in the renal, at times in the iliac artery, especially in that of the left side, the blood current being, it is said, hindered in the right iliac by reason of the passage in front of it of the corresponding vein. More rarely, embolism will occur in the subclavian or in the mesenteric arteries, or in the cœliac axis; it has exceptionally been observed in the bronchial arteries, in the hepatic artery, in the arteries of the bones, of the spinal cord, etc.

If the embolus has taken rise in the peripheral venous system—for example, in the femoral vein—it is readily understood that it will go through the inferior vena cava and, passing through the right heart, will enter the pulmonary artery and stop in the capillaries of the lung. In this way is produced pulmonary embolism in connection with the lesions of the peripheral veins or of the right heart.

Lastly, if the embolus starts from the intestine, it will enter the portal vein and go to the liver; then, if the hepatic barrier is crossed, it will follow the same route as in the previous case. There will be secondary pulmonary embolism.

Such is, as it were, the normal course of an embolus. There are, however, cases in which the foreign body does not follow the blood current. Such are the cases of *paradoxical emboli*.

The embolus, starting from a vein, instead of stopping in the pulmonary vessels, reaches the aortic system. This fact has been explained in two different ways. Weber supposes the existence of particular canals connecting the pulmonary arteries and veins, which canals, being larger than the capillaries, are easily traversed by small foreign bodies. Others have assumed a different mechanism, according to which the embolus, originally very small, passes the lung, then, by a mechanism similar to that of a snowball, accumulates fibrine and acquires a size larger than that of the vessels through which it has passed.

It seems, at present, that another explanation is to be accepted. Since the researches of Zahn, it is established that the foramen of Botal is not obliterated in one fifth of normal individuals (139 times out of 711 hearts examined). A communication, therefore, persists between the two auricles, which fact explains how an embolus can easily pass from the pulmonary into the general circulation.

Finally, there are described, under the name *retrograde emboli*, those whose course is in an opposite direction to the blood current. These are explained by the disturbances produced at the moment of thoracic aspiration, and particularly by efforts of coughing; it is thus

conceived how microbic emboli are quite often engendered in the hepatic veins.

Lymphatic Emboli.—Side by side with blood emboli may well be placed lymphatic emboli. The latter may, from the standpoint of their nature, be divided into mechanical and animate. Among the former, we shall note only the colouring matters introduced beneath the skin by tattooing, and particles of carbon and dust inhaled by the lungs. Being carried into the lymphatic current, these small foreign bodies are stopped in the glands. These organs thus play a protective part for the organism. Their intervention is still more marked in infections; the lymphatic glands often oppose to microbes a very resistant barrier. In the case of malignant pustule, for instance, the disease remains local and curable if the glands corresponding to the inoculated region resist; if they are crossed, blood infection is produced and entails death. Likewise, in tuberculosis, adenopathies tend to prevent the dissemination of the bacilli; in many apparently healthy subjects there are found in the tracheo-bronchial glands tubercle bacilli which remain located there without giving rise to any bad results.

The invasion of the glands, in cases of cancer, is explained by the same mechanism, and finds also its reason for being in a tendency of the economy to circumscribe the disease. Too often, however, the invasion of the glands is the starting point of new lesions; the neoplasia diffuses out of the lymphatic apparatus; in this way cancerous foci may be produced in the pulmonary hilum, consecutively to adenopathies of the same character.

Let us note, finally, that retrograde emboli may occur in the lymphatic as well as in the blood system; they are met with in the thorax, and are supposed to account for certain cases of pulmonary cancer.

Effects of Embolism.—The effects of embolism vary according to the point where stops the foreign body. Arrest may occur in the heart, especially in the right heart. In this case sudden death is frequently observed. A reflex syncope is produced, owing to a violent excitation of the endocardium.

More frequently the foreign body reaches the pulmonary artery. The effects vary with its size.

If its proportions are considerable, the individual may succumb suddenly; a syncope is produced by a reflex action starting from the liver. If the embolus is small, it stops in a branch of the pulmonary artery; the occlusion of the latter is followed by an intraparenchymatous hemorrhage known as *pulmonary apoplexy,* or, still better, *hemoptoic infarctus.*

In the majority of cases the infarcts are multiple, more numerous in the right than in the left, mostly in the lower and posterior parts of the lung. When they are cortical they have the form of a cone whose base is situated beneath the pleura; they are rounded in the interior of the parenchyma. These infarcts are easily recognised by their dark colour, comparable to that of truffles, and by the resistance they offer when palpation of the lung is practised.

Three theories have been put forth to explain their formation. Virchow assumes a diapedesis of red corpuscles, Cohnheim a vascular rupture resulting from the venous stasis. Ranvier, whose opinion is generally admitted, thinks that there occurs a necrobiosis of the arterial wall, and, secondarily, a hemorrhagic sweeping off; it is thus conceivable that there should pass twenty-four to thirty-six hours between the occlusion of the vessel and the hemorrhage.

The pulmonary infarcts are expressed by two classes of symptoms; some of them make us suspect the lesion; the others permit us to affirm its existence.

Among the signs of presumption we will mention dyspnœa, which sometimes assumes disquieting proportions. The physical signs are of little importance: at times a focus of râles with small bullæ is found, and at other times a silent zone surrounded with small râles, and sometimes a murmur is heard.

The true symptom, that which permits recognition of the lesion, is hemoptysis. The sputum of the patient is thick, dark, viscous, non-aerated, adhering to the cuspidor, and exhaling a sour odour comparable to that of antiscorbutic sirup. This expectoration, so characteristic, lasts for five or six days, even when embolism does not recur. It differs considerably, therefore, from the bronchial hemoptysis of the consumptives, which is characterized by the rejection of a red, aërated, spumous blood, and not continuing when hemorrhage has ceased.

It may occur, finally, that the emboli be altogether minute; they occasion in the lungs small punctiform hemorrhages, one interesting variety of which constitutes the festooned diffuse infarctus of Renault. These lesions are not rare in cardiac patients, and are expressed simply by the appearance or aggravation of dyspnœa.

The various lesions produced by the emboli of the lungs may become cicatrized and infiltrated with calcareous salts. At times they are invaded by external microbes, become softened, or even—though this is exceptionally the case—undergo gangrenous transformation.

The effects of *arterial embolism* differ from those observed in the system of the small circulation; they vary also according to the organ under consideration.

In most cases, as already stated, the embolus enters the left common carotid and is stopped in the Sylvian. If the occlusion occurs in the principal trunk, an extensive softening is the result; the hemisphere is transformed, as it were, into pap; the central parts, optic thalami, and corpora striata alone resist, because their circulation is assured by special blood vessels.

In general, only one branch is affected. If it is one of the short arteries, destined for the cortical part of the brain, a superficial patch of cortical softening is formed; if a long artery is struck, the focus occupies the white substance.

Clinical as well as experimental researches permit us to follow very regularly the mode of formation of the lesions. In the beginning a red softening is produced; subsequently, the colouring matter of the blood being transformed, the focus becomes yellow, and finally white. In the end, if its seat is on the surface, it assumes the aspect of yellow, hard, sclerous patches. If it is central, it suffers a more marked softening; the white substance liquefies and presents the appearance and consistency of lime milk; at times the lesion becomes encysted and forms a sort of foreign body.

Large cerebral emboli may give rise to a rapidly fatal attack of apoplexy. Those of medium and small size often produce a transitory apoplexy, followed by permanent disturbances which vary according to the site of the lesion; aphasia and paralysis of the face or the extremities are connected with the cerebral department which has been affected.

Lastly, when emboli are extremely minute, only headache, dizziness, and some mental disturbances are observed; however, should the emboli be repeated, they may entail coma and death.

Of the other arterial emboli, we may cite that of the central artery of the retina, which is expressed by a sudden amaurosis; on ophthalmoscopic examination, the papilla is found pale and the arteries contracted.

If the embolus passes into the abdominal aorta, it may reach the spleen, where it produces an infarctus, expressed by a sufficiently intense pain in the left side. In other instances it stops in the kidney and causes lumbar pain and mild hematuria.

Among the other vessels that may be affected, we will first cite the coronary arteries of the heart. If the embolus is small, it gives rise to angina pectoris, this syndrome appearing whenever cardiac circulation is hindered. If the embolus is more voluminous, the occlusion of the coronary results in sudden death by rupture of the heart.

Finally, when the artery of a limb is obstructed, circulation stops there, the pulse is suppressed, the skin grows cold and pale and is invaded by external germs, which produce in it dry gangrene.

Among the emboli that act mechanically, the fatty and the gaseous deserve special mention.

Fatty emboli are observed consecutively to osseous lesions. When a great traumatism has caused some serious fracture, fat often passes into the blood in considerable quantities; some of it stops in the lung, the remainder invades the general circulation, and may obstruct the vessels of the brain or bulb. Under these conditions a violent dyspnœa is observed, which, after a sudden onset, progressively increases and ends in death. Its differential diagnosis from nervous shock lies in the fact that in the latter case the manifestations are at their maximum at once, while in the former they progressively aggravate.

Gaseous emboli are produced particularly when, in the course of an operation, air penetrates a vein. A characteristic hissing sound is then heard, the patient grows pale, and dies suddenly. If life is prolonged, there is sometimes heard, on auscultation of the heart, a special murmur (the so-called *bruit de moulin*) produced by the mingling of air with the blood.

Generally attributed to obstructions of the pulmonary vessels, the symptoms of gaseous emboli have been ascribed by Brown-Séquard to bulbar emboli. It is certain that when operating upon animals we notice that the gas readily passes through the lung and invades the general circulation. The experiment succeeds well with the dog; by operating slowly one may, without causing any accident, introduce into the veins a considerable quantity of air. After the animal is killed, it is found, at the autopsy, that all the arterial system is filled with small gas bullæ.

Leaving aside the paradoxical and retrograde emboli, we resume in the tabular representation on the opposite page the course and effects of the principal mechanical emboli.

Nervous Connections

Along with functional synergies, contiguity of organs, and vascular relations, we must take into account, as already stated, the connections established by means of the nervous system. After the details given in connection with nervous reactions, we shall only briefly consider this last part of our subject.

The lesion of an organ may, by compressing a nerve, give rise to disturbances in distant parts. A tumour of the mediastinum, an aneurism of the aorta, affecting the sympathetic or the recurrent, produce pupillary or laryngeal disorders, which might lead the inexperienced to an error of diagnosis.

In other instances the question is one of reflex phenomenon, terminating in motor, sensory, vasomotor, and secretory disturbances.

POINT OF DEPARTURE.	ROUTE FOLLOWED.	POINT OF ARRIVAL.	RESULTS.	
			Anatomical.	Clinical.
Lungs, pulmonary veins. Left heart, at times arch of the aorta.	Aorta, left carotid.	Left Sylvian.	Cerebral softening.	Right hemiplegia; aphasia.
	Aorta, right carotid.	Right Sylvian.	Cerebral softening.	Left hemiplegia.
	Aorta, cœliac trunk.	Splenic artery.	Splenic infarction.	Pain in the left side.
	Aorta.	Renal artery.	Renal infarction.	Lumbar pain. Hematuria.
		Iliac artery or femoral artery.	....	Gangrene in the lower extremity.
		Coronary artery.	Infarctus in the myocardium. Rupture of heart.	Angina pectoris. Sudden death.
Peripheral venous system.	Inferior or superior vena cava.	Right heart.	....	Sudden death.
	Vena cava. Right heart.	Pulmonary arteries.	Pulmonary infarction. Punctiform hemorrhages.	Dyspnœa and hemoptysis of dark blood. Asthma-like dyspnœa.
Intestine.	Portal vein.	Liver.	Hepatic infarction.	

Thus, a neuralgia of the trigeminal nerve excites reflexly spasmodic contractions of the facial nerve (or, as is said, *le tic douloureux* of the face). The excitation starting from a viscus, from the biliary or urinary passages, gives rise by reflex action to disturbances in the muscles concerned in the act of vomiting.

The excitation may also produce paralysis or inhibitory acts—e. g., syncope or sensory disorders—which are especially observed in predisposed subjects—for example, in hysterical subjects—and are expressed in their highest degree by a sensitivo-sensorial hemianæsthesia.

We have already repeatedly shown the frequency of vasomotor reactions in distant parts: redness of the cheek in pneumonia, pulmonary congestion in hepatic colic, and the vascular spasm of the myocardium resulting from excitation of the heart, lung, or stomach, and expressed by an attack of angina pectoris.

Do we need to recall, among secretory disturbances, the salivation of gastric affections, the anuria consecutive to abdominal traumatisms, the polyuria or oliguria in sciatic neuralgia, according as the pain is slight or intense? We could cite also various general reactions and psychical disturbances. In all these cases the manifestations seem to have no relation with the organ affected, but are easily explained by the mechanism of nervous reactions.

Résumé.—If we consider in their *ensemble* the various results above recorded, we will understand that a lesion never remains local. As soon as a disturbance is produced, it gives rise to secondary manifestations, which become themselves the starting point of reactions of a third order, etc.

Let us take up an illustration to which we have often referred. A person has an attack of hepatic colic: the local disturbance causes changes in the circulation of the lung; then the heart is influenced, and auscultation reveals an exaggeration of the second pulmonary sound and a right galloping murmur. The heart may become insufficient and dilate; in this manner a little spell of asystole occurs, giving rise to new symptoms, notably to œdema in the lower extremities.

Likewise, it could readily be shown that the kidneys give rise to cardiac disturbances, which in their turn influence the lungs, the liver, and the kidneys themselves.

Thus, the phenomena becoming more and more complicated, clinical types are constituted which are never so simple as might be supposed from the systematic descriptions found in treatises on pathology.

In dealing with a patient, the duty of the physician is, therefore, to trace the succession of the various events. Only by an attentive

study and minute examination is it possible to reconstitute the morbid train and recognise which organ has been the starting point of the phenomena observed.

FEVER

The connections which unite the different parts of the organism account also for the development of general symptoms in the course of the most varied affections. The secretory modifications, the dryness of the tongue, oliguria, respiratory or cardiac disturbances, nervous manifestations, and notably delirium, are to-day easily explained. All these symptoms are due to reflex acts, and especially to the impregnation of the organism with soluble substances.

The same theory is applicable to the changes produced in thermogenesis. Sometimes, and this is most frequently the case, the temperature rises; it is then said that there is *hyperpyrexia (hyperthermia)* or *fever*; sometimes it falls, that is *hypothermia* terminating in grave cases *in algid collapse*.

The expressions hyperthermia and fever are not altogether synonymous. The term hyperthermia means simply elevation of temperature. The term fever is applied to a whole series of phenomena of which hyperthermia constitutes but one element. It implies the co-existence of the thermal elevation with secretory and nervous disturbances.

The distinction is somewhat subtle. Of course, we must leave aside the hyperthermia produced by a sojourn in the oven. But when thermal elevation is of internal origin, the distinction between hyperthermia and fever is difficult to establish. Without dwelling upon this question, which would carry us too far, we shall confine ourselves for a moment to the consideration of the mechanism of febrile hyperthermia.

Is fever, according to the old expression, a heat against nature? For our part, considering morbid phenomena as identical in their essence with normal phenomena, we can not accept such an idea. Fever appears to us to be an exaggeration of natural heat; and this view is corroborated by numerous facts forming a transition between that which might be called physiological fever and that which is designated as pathological fever.

In fact, let us consider the mechanism which explains animal heat and accounts for its regulation. It is known that the temperature of animals is higher than that of the surrounding medium, because living matter, in manifesting its vital activity, renders apparent the heat which it had stored up. The muscles and glands thus disengage a quantity of heat the more marked as their function is the more active.

The digestive canal, as a result of the chemical transformations and microbic fermentations taking place in it, also furnishes the organism with heat.

Heat thus produced is dissipated by cutaneous radiation and by evaporation on the surface of the skin and certain mucous membranes, notably of the mouth.

When the production or the elimination of heat varies, an automatic mode of regulation intervenes; the nervous system increases or diminishes the organic combustions, or, through vasomotor modifications, favours or hinders its loss. At the same time soluble substances, emanating from the cells and tissues, pass into the blood, and, directly or indirectly, through the nervous system, modify the production or the dissipation of it.

However perfect the regulation may be, it may happen, even under physiological conditions, that the organism should fail to maintain a perfect balance. Therefore transitory thermal rises occur as the result of some violent muscular exertion, laborious digestion, painful excitation, prolonged intellectual contention, or emotion. At other times, hyperthermia results from too energetic a reaction—e. g., an individual is suddenly submitted to cold; in order to remedy the loss of heat, the organism calls into play too intense reactions, and the hypothermia produced by the cold is followed by an exaggerated hyperthermia. In order, however, that the nervous system may be capable of raising the temperature by reaction, the excitation must not be too violent; for, in the latter case, inhibitory acts are produced which terminate in coldness and collapse. Nervous shock is a well-known illustration of this eventuality.

If we consider pathology, we see that the different varieties of fever may be brought under two pathogenic groups: *fever by nervous reaction* and *fever by intoxication*.

We shall not dwell upon the former, which we have repeatedly studied. Three varieties of it may be admitted. These are, in the first place, the *algid fevers,* resulting from painful excitation. The so-called hepatalgic fever, accompanying hepatic colic when no symptom points to an infection of the biliary passages, is the best example of such fevers. It has also been experimentally produced in the dog by excitation of the biliary passages. We admit also *reactionary fevers*; consecutive to some hypothermizing action—for example, an individual has ingested carbolic acid; his central temperature falls to 35° C., but a few hours later it again rises and reaches 39° or 40° C. The third variety comprises the febrile movements caused by traumatisms bearing upon certain parts of the *nervous centres*; their reality has been demonstrated by a few observa-

tions, notably by a case of meningeal hemorrhage recorded by Josue, and by experimental researches—for example, those by J. F. Guyon. Hysterical fever may be embraced under this variety.

Fevers of toxic origin are by far the most important. They include three varieties. At times febrile movement is consecutive to the introduction into the organism of completely formed toxic substances proceeding from without. The number of hyperthermizing substances is quite restricted; we shall cite strychnine, caffeine, and curare. At other times, fever is due to auto-intoxication, and, finally, to microbic intoxication.

The existence of *fevers by auto-intoxication* has been demonstrated by numerous experiments and rigorous clinical observations. With this group should be classed the fever of gouty and chlorotic patients, the fever consecutive to the absorption of traumatic sanguineous exudations, and to attrition of tissues, certain forms of fever due to over-exertion, and the fever of asphyxia.

The fevers by *microbic intoxication* evidently constitute the most important class. As all the other infectious manifestations, fever depends, not upon the direct action of microbes, but upon the action exerted by their soluble products.

It must be noted, however, that most of the microbic toxines, when injected in high doses, instead of raising, lower the temperature; they entail death in algid collapse. This result is important, in the first place, because it explains certain clinical facts; then, because it leads to a hypothesis regarding the pathogenesis of fever. It may, in fact, be questioned whether toxo-microbic fever is not due to a reaction of the organism, whether the soluble products of pathogenic agents do not always tend to lower the temperature. If such is the fact, they only excite fever as a reaction of a second order, which expresses a curative effort of the organism. Accordingly, fever is not directly caused by the microbe, but represents, on the contrary, a reaction against hypothermizing substances, and should, when not exceeding certain limits, be considered as salutary. It expresses, at all events, a sufficient energy on the part of the organism, and this view seems perfectly in harmony with facts. One might, in support of this hypothesis, recall the frequency of chills in the beginning and in the course of infectious diseases. Chills represent a mode of reaction to which the organism resorts when it is cold: it is a means of getting warm. Its appearance would therefore be incomprehensible if toxines were heat-producing substances. Nothing is simpler, on the contrary, if we admit that microbic poisons tend to lower temperature; the organism reacts by chills and by hyperthermia. It is well to note, finally, that the gravest and the most rapidly fatal infections lower tempera-

ture.   This is what occurs in cholera or even in choleralike diarrhœas; fever is, in this case, of a good diagnosis.   Similarly, in most of the experimental infections, temperature sinks below the normal when precursory symptoms of death appear: at that moment the organism gives up the struggle and undergoes, without reacting, the action of hypothermizing toxines.

If it is at present easy to conceive the pathogenesis of fever, it is quite difficult to explain its pathological physiology.

It seems demonstrated that thermal elevation results from an augmentation of tissue wasting, but this tissue wasting does not take place in a regular way.   In fact, it is seen from the researches of Dr. A. Robin that if oxidation sometimes increases in simple phlegmasias, it always diminishes under typhoid conditions.

It must therefore be admitted that tissue wasting is vitiated, and this is in harmony with all the results that we have thus far reported with respect to the chemical and toxic characteristics of the blood and urine.

At the same time that the production of heat is increased, its dissipation also seems to be increased.   There is, then, exaggeration of the two normal processes which assure thermal regulation; if the latter is disturbed, it is because production has exceeded dissipation.

Such is the general idea one may form of fever, or, more exactly, of variations in plus or in minus of animal heat.   The history of thermal variations is certainly one of the most interesting problems raised by the study of functional synergies; it is the most remarkable illustration of morbid sympathies.

CHAPTER XX

EVOLUTION OF DISEASES

Evolution of infectious diseases—Incubation: its variations—Invasion—Stationary
period—Local and general manifestations—Different types of fevers—Clinical
forms—Termination of infectious diseases: crises—Convalescence—Relapses—
Recurrences—Passage of infections from an acute to a chronic state—Death
in infections—Evolution of noninfectious diseases—Evolution of intoxications
and visceral infections—Intermittence and periodicity—Latent diseases—Me-
tastases—Recovery and death in general.

WE have repeatedly seen that disease depends upon two factors,
namely, the action of a pathogenic cause and reaction of the organism.
The action is immediate; the reaction may be delayed. Let us con-
sider, for example, the traumatic agents. The effects of these agents
are produced instantly—e. g., fracture, dislocation, or hemorrhage is
observed at once. It has long been recognised, however, that these
are not instances of disease properly so called, and a distinction has
justly been made between wounded and diseased individuals.

Traumatism may, nevertheless, provoke either early or tardy
reactionary manifestations. Syncope or nervous shock develops so
rapidly that the interval between action and reaction—i. e., the latent
period—passes unnoticed. On the other hand, traumatism is the
point of departure of phenomena of cicatrization which are of more
tardy appearance. Cellular proliferations are produced, leucocytes in-
tervene, and thus reparation begins after a certain period of latency.

In studying the physical agents we observe phenomena quite similar
to the preceding. Under the influence of a very energetic agent,
immediate destruction may occur. For example, an ignited mass fall-
ing upon the integuments at once produces carbonization. At the
same time instantaneous reactions are observed. Such, for instance,
are nervous shock or syncope, occurring in individuals falling into
either icy or boiling water, or who have been shocked by an electric
current.

More or less slow reactions are oftener produced by physical
than by mechanical agents. In cases of sunstroke, erythema does

not appear immediately. On the contrary, a certain period of latency elapses between the action of the cause and the development of symptoms.

With chemical agents the effects are still slower. Without doubt certain caustics immediately produce destruction of the tissues, but this is exceptional. In most cases the alterations are slowly produced, as is noticed when a cauterant or vesicant is applied to a patient.

The phenomena are still more striking with toxic substances. If we except a few extremely violent poisons, such as prussic acid, quite a long time elapses between their introduction and their effects.

In cases of slow poisoning—i. e., repeated ingestion of small doses of a toxic substance—disturbances may not appear until the end of several days, months, or even years. The disturbances are manifested not because the dose has been increased, but because cumulative effects and inappreciable deviations from the normal have become apparent as the result of summation.

A period of latency is also observed in acute poisonings. This period corresponds to the time required for the absorption and passage of the poison through those organs which may annihilate it and its arrival at those organs upon which it will exert its action.

In certain instances the phenomena are still more complex. The poison, even when directly introduced into the blood, does not act immediately. Such, for example, is the case with phosphorus. In this instance a secondary *auto-intoxication* is established. The cells, having been disturbed in their function, produce toxic substances which give rise to symptoms. In other words, the poison acts in an indirect manner.

This conception, which is as yet merely an hypothesis, has been extended to microbic poisons. Courmont maintained that the toxine of tetanus modifies the life of the cells, which, acting under its influence, produce a convulsive substance. It is true that this theory has been severely criticised and is not as yet well established, but it is interesting and worthy of note.

Parasitic causes, of which we must here say a word, are never productive of immediate effects. There is always a period of latency during which the pathogenic agent develops. It is for this period that the term *incubation* must be reserved. This expression is not applicable to other processes; it indicates that multiplication of the morbific agents is taking place.

Thus, when a cause acts upon the organism, two events are possible. These are:

1. Immediate effects are produced, as is nearly always the case

with mechanical agents, often with physical agents, and sometimes with chemical agents, but never with animate agents.

2. A period of latency exists which is rare with mechanical agents, frequent with physical and especially with chemical agents, and constant with parasitic agents. In the last case, and in this only, the period of latency should be designated as incubation.

In order to avoid confusion by a too general study, let us first consider a well-defined group and note in what manner evolution occurs in infectious diseases.

EVOLUTION OF INFECTIOUS DISEASES

In the evolution of infections, four stages or periods are generally admitted. These are:

Incubation, which corresponds to the development of the pathogenic agents.

Invasion, which indicates the beginning of reaction on the part of the organism.

Stationary period, during which the disease remains stationary, presenting only more or less marked oscillations of aggravation or amelioration; and

Decline, which is a rather inconstant period.

We will now take up the study of each of these periods.

Incubation.—As already stated, incubation corresponds to the time elapsing between the deposition of a morbid germ in the tissue and the first appearance of local or general manifestations of the disease.

This definition is applicable only to hetero-infections, and must be slightly modified when the process is one of auto-infection. In the latter case the germ is not deposited in the organism from without, and therefore the stage of incubation begins at the moment when the dormant microbe, until then inoffensive, becomes pathogenic under the influence of any excitation whatever. It can readily be understood that if it is difficult to determine the time of incubation in the former case, it is almost impossible to do so in the latter.

During the period of incubation the organism does not always remain passive; on the contrary, it may endeavour to destroy the microbes invading it. Should it fail to do this, however, the disease becomes manifest. It is therefore incorrect to say that infectious disease is a reaction provoked by the introduction of a microbic agent, since morbid reaction does not necessarily occur in all cases. The microbe may be destroyed or remain quiescent at the point where it was deposited. In order that manifestations may appear, a period of preparation is required which represents a first defeat of the

organism. We are thus led to admit the occurrence of three successive stages at the beginning of all infections, namely, introduction or exaltation of the microbe; a latent period of development, corresponding to incubation; and a reaction of the organism corresponding to invasion—i. e., to the beginning of the disease.

The period of incubation may be completely in abeyance and deprived of all morbid manifestation. Then, at a given moment, reaction is produced, often quite suddenly. Such, for example, is the beginning of lobar pneumonia. It is a very curious fact that the microbe should be able to continue secreting its toxines in a progressive degree without provoking any disturbance on the part of the organism, and that the organism should act so tardily when it is, as it were, saturated with soluble toxic products. In other instances the beginning of the disease is manifested in a slow and insidious manner— e. g., as occurs in typhoid fever. Then the transition from a normal to a morbid condition is so insensibly effected that it is difficult to say at what moment the disease commenced.

Even when the beginning is sudden it is often difficult, if not impossible, to determine the time of incubation, since we are not always able to decide as to the moment when contagion has taken place. Most frequently patients are unable to give any information. In the eruptive fevers—e. g., smallpox—it is very rarely possible to determine under what conditions contamination has occurred; in the majority of instances the disease seems to be spontaneously developed. Observations made during three years in the hospital of La Porte d'Aubervillier give a total of 2,304 patients attacked with eruptive fevers. Minute interrogation showed that contagion could be traced in the following proportion: 21 per cent in measles, 12 per cent in scarlatina, 13 per cent in varicella, and 38 per cent in smallpox. Still, the fact remained that, in the majority of the cases, the information obtained was lacking in precision; it was impossible to determine exactly what day contamination had occurred. Finally, in the case of prolonged incubation there is always a question whether there has not been an ulterior contamination which has escaped notice. Consequently, in order to arrive at incontestable results, a series of circumstances that are seldom realized are required.

The perusal of works published on incubation leads to the conviction that an average duration, varying only within narrow limits, exists for the majority of diseases. It would be a grave error, however, to overlook the fact that the period of incubation is at times shortened and at other times prolonged within considerable limits. Nothing in this regard is more demonstrative than the history of venereal diseases; for it is in this class of affections that the moment

of contamination may be determined most exactly and that interpretation is easiest.

With syphilis, for example, it is generally from twenty to thirty days after infecting intercourse that the chancre appears; this average, which is sufficiently wide in its scope, does not, however, include those cases in which infection occurs at the end of ten days, nor those in which it has been delayed until the fortieth or even fiftieth day. The variability of this period is well illustrated by the fact that several indurated chancres, resulting from a single infection, may appear successively in the same individual at intervals of several days.

The same variations occur in gonorrhœa. The average is from two to five days, but the discharge sometimes commences at the end of twenty-four hours or appears very tardily at the end of several weeks. In the latter case it is assumed that the microbes deposited in the balano-preputial furrow had not invaded the urethra until a certain time after coition.

With the soft chancre incubation is more fixed and does not exceed twenty-four hours. This figure is confirmed by numerous inoculations practised upon subjects affected with suspicious ulcerations.

Information is quite precise in cases of infection of traumatic origin.

In the case of tetanus the period of incubation is from two to three days; but there are cases on record in which it is said not to have exceeded two hours. On the other hand, it has also been prolonged to thirty and thirty-five days.

In hydrophobia the incubation period is still more variable, the average being thirty days, and the minimum fourteen. As to the maximum, a period of eighteen months has been admitted, although there are certain cases in which the period of incubation lasted two, three, and even four years.

Erysipelas may be considered as occupying a position between traumatic diseases and those apparently spontaneous. Most of the classic treatises fix its period of incubation at three or four days, admitting that it may be reduced to two days or prolonged to twelve.

In order to determine the duration of the period of latency, traumatic cases must be considered. By an examination of 42 observations we obtain the following figures:

```
Incubation period from   7 to 18 hours .................  6 cases.
     "          "                 24   "    ................. 5   "
     "          "        from 25 to 72  "   ................. 17   "
     "          "           "  4 to  8 days................. 10   "
     "          "           "  10 to 14  "   ................. 3   "
     "          "                 22   "   ................. 1 case.
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In cases of prolonged incubation it may always be questioned whether there has not been a second exposure. However, experimentation inclines us to admit the accuracy of the figures furnished by clinical experience. The inoculation of a few drops of a culture of streptococcus beneath the skin of the ear of a rabbit is followed by the development of erysipelas after the elapse of a period varying from a few hours to eleven days.

The study of nontraumatic diseases yields figures which are far more variable.

Among the eruptive fevers, precise information is most easily obtained in smallpox. Its period of incubation is, on an average, twelve days, but it may vary between seven and fifteen.

In scarlatina, Sevestre finds an almost invariable average of four to five days; but there are observations recorded in which the period of incubation lasted no longer than twenty-four (Trousseau), twelve (Sevestre), and even seven hours (Thomas). In other cases it has been prolonged to twelve, seventeen, and forty days (Rilliet and Barthez). The period of incubation seems to be shorter in surgical or puerperal scarlatina, in which it is hardly three days. This is probably due to the fact that traumatism lessens the resistance of the organism.

The incubation period of measles is from eight to twelve days, with a minimum of four and a maximum of fourteen; that of rubeola is eighteen days; and that of smallpox from thirteen to nineteen days, etc.

Of other infections we may mention diphtheria, which begins from two to four days after contagion, and whooping cough, which appears from the second to the eighth day. It is stated that cholera has at times developed a few hours after contact, and that in typhus the attack has occurred even instantly. In such cases individuals approach a patient, feel a pain which alarms them, and are immediately forced to lie down.

The table on the opposite page, which indicates the average, maximum, and minimum incubation periods, is based upon facts recorded by various authorities, upon statistics published by Williams on behalf of a London commission, and upon our own personal observations.

Clinical experience suffices to establish that the duration of the incubation period is very variable, and experimental researches have demonstrated certain causes which precipitate or delay the beginning of a disease.

Firstly, there is an idea which should never be lost sight of, and that is the variability in the action of viruses. Viruses may be divided into two groups—namely, fixed and variable. In this regard nothing

Incubation

	Average.	Minimum.	Maximum.
Anthrax..................	2 days.	1 day.	3 days.
Chancre, soft..............	1 to 2 days.	1 "	3 "
Cholera	2 to 4 "	1 "	6 "
Diphtheria	2 days.	2 days.	15 "
Erysipelas	4 to 6 days.	7 hours.	22 "
Glanders	3 to 5 "	24 "	3 months.
Gonorrhœa................	3 to 5 "	1 (?) 2 days.	1 to 7 weeks.
Influenza.................	3 to 4 "	1 day.	5 days.
Mumps....................	15 days.	7 days.	30 "
Malaria	6 to 10 days.	99 hours.	Several months.
Measles	8 to 12 "	4 days.	14 days.
Pest	1 to 3 ".	10 hours.	4, 6 to 12 (?) days.
Rabies	20 to 60 "	13 days.	18 months.
Rubeola	18 days.	5 "	21 days.
Scarlatina................	4 to 5 days.	7 hours.	7 weeks.
Smallpox.................	12 days.	7 days.	15 days.
Sudor anglicus...........	2 to 3 days.	24 hours.	(?)
Syphilis	20 to 30 "	10 days.	50 days.
Tetanus	2 to 3 "	2 hours.	35 "
Typhoid (fever)...........	14 days.	2 days (?)	21 "
Typhus	12 "	(?)	23 "
Vaccinia	3 "		
Varicella	14 to 15 days.	13 days.	19 "
Whooping cough..........	8 days.	2 "	8 "

is so instructive as the history of rabies. The variable virus is that found in an animal which has accidentally become rabid (*rage des rues*); the fixed virus is that which has acquired a definitely determined power by virtue of successive passages through animals. By inoculating the virus into animals of the same species placed under the same conditions, the phenomena are made to appear after the elapse of a perfectly determined period of time. Such is not the case, however, in Nature, and the constant variations in virulence lead to modifications in the incubative period.

The same result is observed in man. By virtue of its transmission by successive inoculations, vaccine has become a fixed virus; its period of incubation is well-nigh invariable. In subjects vaccinated for the first time the eruption begins seventy-two hours after inoculation, and is well developed in the course of the fourth day. Even with this fixed virus, however, certain variations are observed. Dr. Saint-Yves Menard has kindly furnished us with interesting information upon this subject, which is as follows: The incubation period of vaccination quite often lasts four to five days, exceptionally six or seven. In this respect the following is a very curious result: Children are returned seven days after vaccination with a negative result; they are vaccinated a second time, and in certain exceptional cases the first punctures as well as the second will be seen to be followed by the simultaneous development of pustules eleven days after the first inoculation. It

is thus seen that the vaccine virus is but slowly destroyed, and if the organism be profoundly modified by a new inoculation, such will suffice to cause the development of germs which seemed to have been destroyed.

The soft chancre, which is transmitted by direct inoculation, has also acquired a sufficiently fixed power, exactly as in the case of experimental virus. Therefore the lesion always begins to make its appearance twenty-four to forty-eight hours after infection. The occurrence of a longer period of incubation must be attributed to inaccurate observation.

It can readily be understood that with viruses of variable potency the incubation period will be the shorter the greater the energy and number of microbes introduced.

The period of incubation will also vary with the location of the wound. It will be longer if the affected region is provided with a dense cellular tissue and is poorly supplied with vessels and nerves. Such is strikingly the case in rabies.

Finally, microbes develop more readily when they are introduced simultaneously with agents favouring their multiplication, such as irritating substances or other bacteria, even though the latter be simple saprophytes.

As to the organism, all causes of weakening should be taken into account—extensive traumatism, laceration of tissues, modifications of the general condition by overexertion, excesses, alcoholism, intoxications, and previous and present diseases. Lastly, we must not overlook the influence of moral impressions, whose power is well known with respect to rabies. For example, an individual who has been bitten by a rabid animal no longer thinks of his accident. All at once a word reminds him of the bite, and immediately manifestations of rabies appear and rapidly end in death.

The duration of the period of incubation may also be modified by the responsive aptitudes of the subject. In persons with very sensitive nervous systems, the onset will be hastened. In this particular case a short incubation period constitutes a favourable phenomenon.

Invasion.—Invasion may be sudden, or slow and progressive. In the former instance the stationary period is quickly reached; in the latter it supervenes only at the end of a few days, and is thus preceded by a prodromic period in which the symptoms are inadequate to determine the nature of the morbid process.

As an example of infection with sudden onset, writers always cite pneumonia, and as an example of slow invasion, typhoid fever. These two illustrations are well chosen. Clinical phenomena are always so

variable, however, that exceptions may be mentioned. There are cases of pneumonia beginning in a slow and insidious manner, as often occurs in the aged; and there are typhoid fevers which are manifested by a sudden onset, as is sometimes the case in children.

It is not difficult to understand how a progressive invasion is effected. The noxious substances are secreted little by little by the microbes, become diffused in the organism and influence the cells; when the toxines are produced in greater amount, their constantly increasing accumulation gives rise to more and more marked disturbances.

A sudden onset is more difficult to explain. Even in pneumonia it is possible that the morbid poison is secreted in a progressive manner, and at first sight the sudden appearance of the phenomena is not understood. The differences are probably due to the mode of action of poisons. This view is, of course, purely hypothetical, but it is supported by some facts. A first result which must be taken into account is that most microbic toxines, like the poisons properly so called, and notably alkaloids, exert no immediate action. Even when they are introduced into the blood no immediate symptom is produced, but after a period of latency of varying duration the morbid phenomena suddenly appear. This experimental result has a very important bearing upon our subject. In fact, it may be assumed that in certain cases microbic poisons act early and rapidly as they are formed. Under such conditions, disturbances begin slowly and follow a progressive course. In other instances an oversaturation of the organism will be required in order for reaction to be produced. This is the first effect of cumulative doses.

Whatever be the mode of invasion, the general phenomena first bear on the nervous system. If invasion is slow and progressive, the disturbances are accentuated little by little. These are malaise, headache, dizziness, weakness of the extremities, and incapacity for all muscular or mental exertion. Delirium, if present, is of the mild, quiet type. Sleep is disturbed only by nightmares or vagaries. On the whole, the symptoms are not intense, but are established gradually and aggravated in a slow and often regular manner.

On the other hand, if invasion is sudden, the nervous symptoms will be intense and disquieting from the first. In fact, the process is of the nature of a true outbreak. These has been a silent accumulation of toxines, and all of a sudden a violent, impetuous, unexpected reaction occurs—i. e., intense chills or, in children, a convulsive attack. At the same time fever develops and rapidly reaches 39° or 40° C. Headache is intense, and delirium may be excessive from the first. Severe delirious phenomena are mostly, we might say

nearly always, observed in diseases characterized by sudden onset and occurring in predisposed individuals. Delirium tremens is altogether exceptional in typhoid fever; it is not so rare in smallpox and erysipelas, but it is especially frequent in pneumonia. It expresses a profound nervous perturbation, and occurs in alcoholic subjects as the result of a toxomicrobic shock—such, for instance, as is induced by violent traumatism.

Likewise, in diseases characterized by sudden invasion, a series of symptoms which might, perhaps, be connected with visceral lesions, but which seem to be dependent upon a disturbance of innervation, is observed from the very beginning. These are, vomiting without any apparent alteration of the stomach; diminution in the quantity of urine, at times transitory suppression, without the kidneys as yet being affected; intense dyspnœa, unexplained by the condition of the lungs; acceleration of the pulse, and arrhythmia, which are in nowise dependent upon cardiac lesions. There is a striking discord between the functional and the anatomical conditions.

Thus far we have considered only the general symptoms. The local manifestations may appear from the beginning; at times they precede the general reactions, sometimes they accompany them, and sometimes they run their course without giving rise to any general phenomena.

In most cases the local lesions present a course which, even when rapid, is generally progressive. In cases of phlegmon or erysipelas, as well as in those of pneumonia, it is possible by means of inspection or auscultation to follow the extension of the process.

Sometimes, however, the local lesion develops almost instantly. This occurs in young subjects endowed with a nervous system reacting quickly and energetically. Such, for instance, is observed in children in conditions described by clinicians as acute pulmonary congestion. The child is suddenly seized with fever, and auscultation practised immediately reveals an intense blowing murmur. On the following day everything is again all right; the fever has subsided, the murmur is no longer perceptible. These facts, which have been so well studied by Bergeron, Cadet de Gassicourt, and Hirne, must at the present day be considered as examples of veritable abortive pneumonias. Immediately upon its arrival the microbe gives rise to violent reactions, which often result in the instant arrest of its course. The excitation of the nervous system is expressed by a congestive fluxion which arrests the infection. In the same order of ideas, although their meaning is more difficult to understand, we may mention herpes, which is so frequently observed in infections, and urticaria, which appears especially in cases of digestive disorders.

Evidently the phenomena of fluxion are alone capable of making a sudden appearance; the other reactionary symptoms develop more slowly, and if at times they appear suddenly it is because their beginning has been effected in a gradual manner, and, having already advanced to a certain degree, they become manifest only when they abruptly provoke morbid reactions.

There is often a lack of harmony between general and local manifestations. In a certain number of cases the two orders of symptoms begin simultaneously and manifest the same mode of invasion; in others the disease is at first characterized by one or the other series of symptoms; in still other instances local reactions are progressive, while general manifestations are abrupt, and *vice versa*. There exist, therefore, a whole series of different modes of action of which clinical experience furnishes well-known examples.

Stationary Period.—Since the time of Hippocrates it has been the custom to admit three periods or stages in the evolution of acute diseases: an invading period, a stationary period, and a period of decline. Jaumes has proposed another division. He admits but two periods—namely, one characterized by a morbid effort corresponding to the period in which the organism appears to be overwhelmed; and one occurring only in favourable cases—i. e., a period of improvement and restoration. In other words, the first period corresponds to the attack by the pathogenic cause, and the second to the curative effort of the organism. This division is quite in harmony with the present-day conception of disease. It would have been perfect if reaction really followed action, and if disease followed a regularly descending course after arriving at its height through a progressive aggravation. In reality the facts are more complex. As we have repeatedly stated, the defensive reactions begin at the same time as the offensive actions, and at times even before all appreciable symptoms. Consequently, the two classes of symptoms constantly intermingle, with the exception, however, that the pathogenic agent has the advantage in the beginning. The reactions of the invasion period indicate that the organism is defeated, or at least on the defensive. Then comes a period when the struggle assumes a serious character, and the two participants fully display their forces. This is the stationary period, which at times seems to remain unchanged, and at others to present a series of deviations depending upon the various vicissitudes of the struggle. This period is the most important from a nosological standpoint, since the characteristic symptoms of the disease are well developed; they are so grouped as to constitute a special type, which is easily defined and classified. It is at this time that a previously hesitating diagnosis may be made more certain.

In studying the stationary period, the local symptoms and general phenomena must likewise be taken into consideration.

When the local manifestations occupy the external parts, they may easily be studied. Such is the case with erysipelas, abscesses and phlegmons, cutaneous ulcerations, and gangrene. These also are quite easily recognised when they occupy a mucous membrane which can be readily explored, such as that of the mouth and pharynx. In case a deeply seated organ is attacked, the study becomes more difficult; yet, according to the modifications manifested in the functions of the organ and the changes which may be perceived by means of physical examination, palpation, percussion, and auscultation, we can quite exactly determine and follow the evolution of the phenomena produced in the deeper parts of the economy.

In certain instances even the minutest examination fails to reveal any organic alteration, because the symptoms are of a general character. The latter consist in reactionary manifestations referable chiefly to the nervous system, the secretions, and thermogenesis.

The nervous symptoms are those which have already been noted in treating of the invasion period—namely, headache, incapacity for work, a diminution of psychical acuity, delirium, and, exceptionally, convulsions. The secretions are for the most part diminished; the urine is scarce, the saliva is not abundant, and the tongue is dry. Finally, thermogenesis is also perverted, and there is usually a rise of both peripheral and central temperature.

A comparison of local and general symptoms leads to the following conclusions:

Sometimes the local and general phenomena follow a parallel course. They are aggravated or diminished simultaneously; they decline and disappear almost at the same time. Sometimes there is a decided discord between the two orders of manifestations. Thus, for instance, the local lesion may subside, while the general symptoms grow worse. In such cases there is generally some fresh complication. More frequently the reverse is the case, the general phenomena vanish, whereas the local manifestations seem to remain stationary. This fact is particularly striking in pneumonia. From one day to the next a sudden defervescence occurs; the temperature, which had risen to 40° C., falls to 37° C.; the secretions are re-established; the patient experiences a feeling of well-being which makes him realize that his sickness is over, and yet no improvement has taken place in the condition of the lung; on the contrary, the stethoscopic signs are the same as the day before. The same lack of parallelism is observed in erysipelas, but not constantly; the general phenomena subside, while the cutaneous lesion persists without any change.

Finally, in certain cases the discord is no longer real, as in the preceding examples, but only apparent. The local lesion seems to remain stationary, and yet the general phenomena are modified or aggravated. These indicate either a local change, which we are thus permitted to recognise and predict, or a new perturbation, perhaps a commencing complication.

In order to recognise the nature, follow the evolution, establish the prognosis, and predict the possible accidents of a disease, we must at the same time note its local and general manifestations, and their harmony or discordance.

Let us first consider the *local phenomena*. Five results are possible:

1. The local lesion, which has begun during the period of invasion, is not modified during the stationary period, but follows a very simple course, increases gradually, reaches its height, and then, in favourable cases, declines. But no notable change in its character or aspect appears.

Of numerous illustrations it will suffice to mention mumps, erysipelas, and gonorrhœa. We might add scarlet fever and measles, in which the eruption characterizing the stationary period extends progressively to all parts of the skin, but always preserves an invariable aspect.

2. In other cases the local lesion is modified from day to day. As an example in which observation is easy, an abscess may be taken. At first induration is found, then the lesion undergoes softening, becomes fluctuating, and opens exteriorly. A like course may be observed in cases of visceropathies. In simple bronchitis there is a period of crudity when expectoration is difficult and painful; then a period of coction, when the sputa become mucopurulent and are easily thrown out. Examination of the sputa, as well as auscultation, demonstrate the changes characterizing these two periods. By the same methods of exploration we can follow perfectly the evolution of a pneumonic focus: In the beginning there is pulmonary obstruction resulting from the exudations, and auscultation reveals crepitant râles; next, a fibrinous exudation into the air cells takes place—this is the period of red hepatization, characterized by tubal breathing; finally, the exudation softens and auscultation reveals râles of resolution (*râles de retour*).

3. Instead of remaining localized, the local lesion extends and invades the neighbouring parts. Here erysipelas and pneumonia may again serve as examples.

While often circumscribed, erysipelatous inflammation sometimes extends to a great part of the skin. At times it covers the entire

surface of the body. This is a particular clinical form justly described under the name ambulatory erysipelas. The same evolution may be observed in the lung, under which circumstances pneumonia is designated as migrating.

In certain but fortunately very rare cases a local lesion grows both deeper and larger, causing considerable loss of substance. This is what constitutes *phagedenism*, observed mainly in the soft chancre, which lesion may destroy the penis, invade the scrotum and thighs, and follow a serpiginous, extensive course, the duration of which may be months or even years.

4. The local lesion sometimes progresses by successive stages. At a moment when the lesion seemed on the point of subsiding or had even disappeared, a renewal sometimes occurs in the region primarily attacked. This is observed especially in erysipelas. At times the renewal occurs in parts more or less distant from the region primarily affected—for example, the orchitis occurring in mumps, and endocarditis, pericarditis, or meningitis of pneumonia. The pathogenic agent thus tends to colonize distant tissues or organs: it is, as it were, a relapse at a distance.

5. Finally, the local lesion may be modified by an additional infection. Pathogenic microbes implanting themselves, for example, in a part already diseased, give rise to suppuration, and may even invade the economy. In gonorrhœa the gonococcus remains localized in the urethra; common bacteria, however, soon join it, and may subsequently provoke very serious disturbances. Although the gonococcus may sometimes invade the organism, the so-called gonorrhœal rheumatism nearly always depends upon ordinary pyogenic bacteria. The process is one of attenuated purulent infection, to which the agent of gonorrhœa has merely opened the way.

General phenomena usually follow a course parallel to that of local manifestations. During the stationary period they may remain quite unmodified. In pneumonia, for instance, the fever remains about 40° C. Dyspnœa, thirst, and headache remain about the same during the entire evolution. The same remarks are true of typhoid fever, although some differences are revealed by a more careful study.

In some cases the general symptoms are modified several times, so that the stationary period permits of division into a certain number of secondary periods. In other instances the general symptoms keep pace with the local, as is observed in smallpox.

Sometimes the changes do not seem to harmonize. Thus, in tubercular meningitis three periods, which apparently do not correspond to anatomical changes, have been described according to the general symptoms. After a phase characterized by violent headache, fever,

constipation, and vomiting, a marked remission occurs, which lasts nearly a week; the patient is believed to be convalescent, when the symptoms are renewed, and go from bad to worse, ending in death.

In a certain number of infections the modifications in the general symptoms express the generalization of a primarily local microbic process. Such is the case with the malignant pustule. The lesion is at first characterized simply by a cutaneous eschar; thus, in certain cases, phenomena of general infection are subsequently produced, indicating the invasion of the economy by the pathogenic agent. Likewise, in cases of septicæmia or pyæmia consecutive to local lesions, the changes occurring in the general symptoms reveal the invasion of the organism.

Nosologists have divided the stationary period of diseases by taking into account both the modifications occurring in the local symptoms and the general manifestations. Undoubtedly, these divisions are not always perfect. Didactic descriptions are necessarily schematic and can not give an exact idea of the complexity of clinical phenomena. We have above referred to tubercular meningitis. Its evolution in three phases, admitted by all the classical treatises, is, however, quite rare. The phenomena very seldom, if ever, progress with such quasi-mathematical precision as has been attributed to them. The clinical types are, in reality, far more complex and variable than may be supposed from the classical descriptions.

Notwithstanding their variability, general phenomena evolve according to four types. Types have been divided into continued, remittent, intermittent, and irregular, mainly upon the basis of the precise data of medical thermometry.

The *continued type* is represented by the cases in which the symptoms, after having reached the stationary period, do not present any change from one day or one moment to another; the condition remains the same. The classical example is typhoid fever, which disease is often called *continued fever*. However, on looking into the matter more closely, it may readily be recognised that the continuity is not perfect; a series of variations is constantly produced which have rightly led clinicians to look upon the so-called continued fevers as remittent fevers. Every morning the temperature is a few tenths of a degree lower than on the previous evening, and the general manifestations, although continuing grave, are slightly attenuated. These variations are nothing else than an exaggeration of normal phenomena. In fact, in health the temperature is modified at different hours of the day; it describes a regular curve, whose minimum is between 3 and 5 A. M., and maximum between 4 and 7 P. M.; the difference between the two figures is, on an average, 0.8° C. In

typhoid fever, the morning temperature usually varies between 39.5° and 40° C.; that of the evening, between 40° and 41° C., the difference being from half a degree to one and a half. But it may sometimes become more notable. Later on the remissions are accentuated, as is observed at the end of the disease. Quite frequently there will even be seen at this period great variations tending to bring the morning temperature to a normal. This is what is called the *amphibolic stage*.

When the remissions become considerable the temperature at certain moments returns to the normal figure. The fever is then called *intermittent*.

The intermittent fevers are often divided into two great groups: the malarial intermittent fever and the symptomatic intermittent fevers.

Paludal fever, or *malaria*, is intermittent because, it is said, the parasite which causes it—Laveran's hematozoon—periodically invades the blood of those affected; the symptoms then become manifest, and are characterized by the three classical stages of chills, fever, and sweats. The parasite then takes refuge in certain organs—in the spleen and in the marrow of bones—and then the febrile paroxysm subsides. The fever will reappear upon a new incursion of the parasite. This theory is doubtless too simple, since the parasites are often found in great numbers in the blood after the end of the paroxysm. This pathogenesis has been easily admitted for the reason, perhaps, that it is difficult to formulate another, perhaps also by analogy with recurrent fever. In the latter case, the presence of spirilla in the blood exactly coincides with the development of the paroxysm.

The symptomatic intermittent fevers differ from the malarial in that their paroxysms are less regular. Contrary to what occurs in malaria, the fever generally returns in the evening, is sometimes repeatedly reproduced during the same day, and reappears at different hours on the day following. These paroxysms should always arouse the suspicion of a suppurating focus in the viscera. They are particularly frequent in suppurative hepatitis, angiocholitis, urinary infections, and ulcerating endocarditis, and almost constant in purulent infection. Despite their intermittent course, they are connected with progressively growing lesions; they are intermittent, although the evolution is continuous.

This discordance is difficult to explain. It may be supposed, however, that the toxines liberated by the suppurating focus act only after a certain incubation—that there is produced a phenomenon similar to that occurring in cases in which an infection begins suddenly. The paroxysm is the result of cumulative doses and the febrile

reaction is probably connected with elimination of noxious substances; the symptoms reappear when a new accumulation is produced.

Whatever may be the explanation, febrile intermission is only an exaggeration of physiological remission. All fevers are not freely intermittent, probably because each paroxysm begins before the previous one is terminated; according to this hypothesis, remittent fevers should be considered as intermittent. In this way, it is very readily understood that on certain days very marked remissions might occur even in continuous fevers. This is frequently observed in typhoid fever, notably toward the fourteenth day, sometimes the sixteenth or the nineteenth.

Clinical Forms.—The stationary period of infectious diseases, being the longest, and especially the best characterized, has served to differentiate clinical types.

On the basis of their evolution, cyclical diseases may be admitted in which the duration is sufficiently defined and is determined by a regular succession of morbid phenomena. Pneumonia, typhoid fever, and eruptive fevers belong to this category. However, it should be remembered that the figures given by authorities are subject to numerous variations. The term of nine days assigned to pneumonia, and of three weeks to typhoid fever, represent averages which are seldom realized.

Nevertheless, the term may be retained in contradistinction to noncyclical diseases, such as diphtheria or erysipelas, whose capricious course defies all efforts at averaging.

Even in those diseases in which the stationary period is best determined, very great variations may be observed.

In certain cases the evolution is shortened, either because the disease assumes a subacute, speedy course, causing death very rapidly, or, on the contrary, because it follows an abortive course. Pneumonia is again a good illustration. This infection, produced by the classical pneumococcus, may kill in certain instances within a few hours. This happens in the aged, in diabetics, and in individuals suffering with previous diseases, particularly erysipelas.

In this connection we may also mention the speedy types of scarlatina, smallpox, and cholera. Death may occur at the beginning of the stationary period, and even before the latter is clearly established.

Pneumonia also furnishes the best example of an *abortive infection*. The disease begins suddenly, reaches the stationary period, and all at once defervescence becomes established toward the third or fourth day. Abortive typhoid fevers have also been described, and we may also admit the occurrence of abortive fevers—i. e., such as are cut short after a prodromic period. Thus, an individual who has been

exposed to the contagion of smallpox is seized with all the premoni-
tory symptoms of this disease; then the symptoms disappear and the
eruption is characterized by two small pustules. This is evidently an
instance of an attack of smallpox deserving the name abortive. Not-
withstanding the intensity of the symptoms of invasion, the disease
is cut short. Cases of abortive erysipelas which stop suddenly after
the period of invasion at the very beginning of the stationary period
may also be admitted. It is useless to multiply examples. While
these facts are already well known, we believe them to be far more
frequent than is usually supposed. Many febrile paroxysms, transi-
tory malaises, and sudden chills, which are followed by no special
manifestations whatever, and which run their course in a day and
sometimes in a few hours, are to be accounted for by an infection that
is aborted. Consecutive to infections occurring during convalescence
from eruptive fevers or erysipelas, we often see febrile paroxysms,
which, it seems, are referable to no other cause. This is demonstrated
by the fact that numerous transitions are observed between the ephem-
eral fevers, which can in no wise be accounted for, and those which
indicate a relapse or a complication. Lastly, the diseases aborting
spontaneously should be placed parallel with those aborting in conse-
quence of therapeutic intervention. Cases of this kind, formerly rare,
will become more and more frequent as we become better acquainted
with specific medicaments. The latter are sometimes represented by
vegetable or mineral products. Such are the salts of quinine, which
arrest the malarial infection; the salts of silver, which stop a begin-
ning gonorrhœa; and especially the preparations of mercury, which
suspend the evolution of syphilis. At present specific and abortive
remedies are looked for in substances derived from immunized ani-
mals. The results obtained by serotherapy inspire us with the hope
that the time is not far distant when it will be possible to arrest the
evolutions of a great number of infectious diseases.

The acute infectious diseases, even when they follow a cyclic
course and terminate within a well-determined time, may in some
cases be prolonged beyond the usual limits. For instance, pneumonia,
instead of lasting nine days, may not reach defervescence until toward
the twelfth or even the fifteenth day. Likewise, typhoid and eruptive
fevers are not infrequently prolonged in an unusual manner, although
examination of the patient fails to explain the persistence of the
morbid symptoms. There is, so to say, a torpidity of the organism
which does not succeed in producing the special conditions capable of
arresting the infection.

In a great number of cases, however, prolongation of the disease
is due to a particular course or to the influence of complications.

The evolution is prolonged as the result of *successive invasions*. At the moment when the infection is believed to be nearly terminated a new focus is produced. Pneumonia and typhoid fever may evolve in this manner, and although the new attack is generally of shorter duration than the first, the total duration is thereby considerably prolonged. This mode of evolution, while rare in the diseases above referred to, is the rule in certain infections, such as recurrent typhus and intermittent fever. Such is precisely the case with varicella, the duration of which is extremely variable on account of the variation presented by the course of successive renewals.

In certain cases the renewal of morbid symptoms is preceded by an interval of recovery; then it is said that there is a recurrence. As in the case of relapse, *recurrence* also is generally less grave than the first attack; but this rule offers a great number of exceptions.

Finally, morbid evolution may be prolonged by *complications* occurring during the stationary period or convalescence. New phenomena, mostly due to superadded infections, may thus lengthen the duration of a disease for a very long time.

It is evident that nothing but hypotheses can be advanced as to the causes which intervene to abridge or prolong infections. Aside from those cases in which secondary complications are produced, it is not understood why the morbid action is cut short, and then reappears at the moment when defervescence was about to set in, or even after the beginning of convalescence. The solution of these problems is intimately connected with the study of predisposition, immunity, and the mechanism of recovery. If, as is generally admitted, recovery is effected by virtue of chemical and dynamic modifications produced within the organism; if it is dependent upon an increase of the germicidal power of the tissue fluids and upon the phagocytic activity of the cells, the duration of the disease will, of course, depend upon the rapidity of the organic changes—namely, upon the reactionary power of the organism. Relapses, on the other hand, would be due to an insufficiency of reaction. This explanation, however, is inadequate. What we desire to know is the conditions which cause the economy to react promptly in one case, slowly in another, and incompletely in a third. The question is thus reduced to a problem of a much more general nature. We have seen that the various morbid reactions are in part dependent upon the nervous system, and in part due to the state of general nutrition. They vary notably from one subject to another, and this variability is in relation with the hereditary or personal antecedents of the individual, with his special innate characteristics and idiosyncrasies; in other words, with the different causes to which we have constantly referred to explain the development and course of diseases.

Reactionary differences also explain the differences of *termination*. When reaction is energetic and timely, it succeeds in destroying the invading microbes; if slight or slow, it only arrests their progress and the process passes into a chronic condition; if too weak or too tardy, it fails to save the organism, and the disease terminates fatally.

These considerations suffice to demonstrate that the same infectious disease may present varied symptoms and follow an extremely variable evolution. Supposing all conditions to be the same as far as the microbe is concerned, the influence of the organism makes itself constantly felt and contributes to modify the scene. Therefore a certain number of clinical forms have been admitted. These divisions are evidently quite arbitrary. In order to establish them, the various cases encountered have been compared with an habitual average type, running its course without the intervention of any unusual influence. In this way clinical forms have been grouped under two heads: First, according as modifications depend upon some anomaly in the course, or in the morbid symptoms, or in localization; or, second, according as they are due to the condition of the subject. With some variation this division may be applied to all infections.

In order to fix the ideas, let us consider the two diseases in which clinical types are the most numerous and the most varied—i. e., pneumonia and typhoid fever. The two following tables will show how clinical forms may be classified; the terms sanctioned by usage are clear enough to make description unnecessary.

Clinical Forms of Pneumonia

I. DIVISIONS BASED ON THE STUDY OF THE DISEASE.

    1. *According to the course.*

        Abortive pneumonia.
        Speedily fatal pneumonia.

        Prolonged pneumonia ⎰ Double.
                           ⎨ With successive foci.
                           ⎩ Migrating.

        Infecting pneumonia.

    2. *According to the morbid elements or symptoms.*

        Inflammatory pneumonia.
        Adynamic pneumonia.
        Ataxic pneumonia.
        Pneumonia with icterus.
        Bilious pneumonia.

    3. *According to localization.*

        Pneumonia of the base.
        Pneumonia of the apex.
        Central pneumonia.
        Massive pneumonia.
        Pleuro-pneumonia.

II. Divisions based on the Condition of the Subject.

1. *According to the age.*

> Pneumonia of children.
> Pneumonia of the aged.

2. *According to the previous state of health.*

> Pneumonia of cachectics.
> Pneumonia of drinkers.
> Pneumonia of the obese.
> Pneumonia of diabetics.
> Pneumonia of bronchitics.
> Pneumonia of the tubercular.
> Pneumonia of those suffering with malaria, etc.

3. *According to the coexistence of another infection.*

> Pneumonia of typhoid fever.
> Pneumonia of erysipelas.
> Pneumonia of acute articular rheumatism, etc.
> Pneumonia of influenza.

Clinical Forms of Typhoid Fever

I. Divisions based on the Study of the Disease.

1. *According to the course.*

> Abortive typhoid fever.
> Prolonged typhoid fever.
> Speedily fatal typhoid fever.
> Typhoid fever with relapses.

2. *According to the morbid elements.*

> Mucous typhoid fever.
> Ambulatory typhoid fever.
> Inflammatory typhoid fever.
> Bilious typhoid fever.
> Hemorrhagic typhoid fever.
> Ataxic typhoid fever.
> Adynamic typhoid fever.
> Putrid typhoid fever.
> Hyperpyretic typhoid fever.
> Sudoral typhoid fever.

3. *According to the localizations.*

> Nervous forms $\begin{cases} \text{Meningeal.} \\ \text{Spinal.} \end{cases}$
> Thoracic form.
> Gastric form.
> Icteric form.
> Renal form.
> Cardiac form.
> Septicæmic form.

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II. Divisions based upon the Condition of the Subject.

1. *According to the age.*

Typhoid fever of children.
Typhoid fever of the aged.

2. *According to the previous condition of health.*

Typhoid fever of cachetics.
Typhoid fever of the obese.
Typhoid fever of drinkers.
Typhoid fever of the tubercular.

3. *According to the coexistence of another infection.*

Typhoid malaria.
Laryngo-typhus.
Pneumo-typhus.

Termination of Infectious Diseases

We have repeatedly shown that the organism is provided with means of protection which prevent the penetration and multiplication of pathogenic germs. The latter may succeed in invading the economy only when the vigilance of the cells is distracted for a moment and the humours are altered by some affection. Then the disease manifests itself. Modifications in the cellular nutrition are immediately produced, however, which transform the blood, the humours, and the tissues, and make of them culture media nonadapted for the pathogenic agent. Now, two results are possible. In some cases the changes are produced slowly and progressively; the organism gradually rids itself of the germs and neutralizes the action of the toxines which impregnate it. Defervescence is produced in a slow manner; the fever diminishes progressively, by *lysis*, and the various functions consume a more or less long time in returning to their normal condition. It is therefore possible to follow the progress of recovery day after day. This is what takes place in typhoid fever.

In other cases, on the contrary, the termination is abrupt and sudden, as in pneumonia. It is then said that a *crisis* has occurred.

Crises.—From the earliest antiquity it has been noted that certain diseases may present sudden changes in their evolution. This is *crisis*, which supervenes when the peccant (corrupt) humour has undergone coction; Nature expels it from the body or causes its deposition in some part of the organism. The latter result was formerly considered fortunate or unfortunate, according as deposition occurred in an organ of little importance or indispensable to life. These ideas led Hippocrates to formulate the following definition: "A crisis in diseases is either an exacerbation, a decline, a metaptosis, another affection, or the end."

The crisis, however, did not occur at undetermined periods; it appeared on fixed days, called *critical days*, which corresponded to weeks or half weeks—that is to say, to the fourth, seventh, tenth, fourteenth, seventeenth, and twentieth days. The critical days were preceded by the *indicating days*, when an exacerbation of the symptoms was usually observed. It may be added that Hippocrates did not regard the critical days as possessing an absolute value; the crisis might occur twenty-four hours sooner or later. Galen, on the contrary, attributed to each day an absolute significance. He argued that acute diseases did not last more than forty days, and considered the crisis as a sudden reversion to health.

The latter definition has prevailed. At the present day the name crisis is reserved for the *ensemble* of favourable changes occurring suddenly in morbid evolution.

One of these changes is that of the temperature, which in the course of one night falls from 40° to 37° C. In some cases the thermal reduction is excessive. The thermometer marks 36° or 35° C., and this hypothermia sometimes occasions disquieting phenomena, especially in the aged; it is attended with collapse, and demands intervention for restoration of heat to the patient.

With the fall of the fever the secretions are re-established; the skin becomes moist and the urine abundant. On the previous day the patient may have voided 500 to 600 grammes; after the crisis diuresis may reach 2, 3, and even 4 litres. But what is still more notable, perhaps, is the feeling of well-being experienced by the subject. As the crisis usually occurs during the night, it is surprising to find the individual, who was left in a condition of great suffering on the previous evening, completely cured on the following morning. The local phenomena, however, have not changed. If the case be one of pneumonia, the physician finds the same stethoscopic signs as on the previous day; if a case of erysipelas, he observes that the cutaneous lesions have not improved.

Modifications which might lead the inexperienced to error may be observed in the circulatory apparatus. On the previous day the pulse may have been rapid and weak, but regular; at the moment of crisis it becomes strong and slow, but at times irregular and unequal. This phenomenon is observed especially in children, and probably depends upon a nervous disturbance, which is of no grave significance.

The sudden and profound changes occurring at the moment of crisis may occasion new nervous reactions—e. g., convulsions in children and delirium in adults. There are cases on record in which a paroxysm of delirium tremens developed at the moment of defer-

vescence of a pneumonia. These disturbances, though sometimes alarming, are generally without gravity.

Among other critical manifestations, transitory erythemata, outbreaks of urticaria and herpes, sometimes diarrhœa, a bilious attack, or epistaxis, may be mentioned.

Special attention has been devoted to changes presented by the blood and urine.

Dr. Hayem has described a *hematic crisis* in which the white corpuscles, increased in number during the disease, return to their normal number. The red corpuscles have been progressively diminished, and at the time of the crisis an activity on the part of the hematoblasts occurs, designed to increase the red globules.

The *urine* has been the subject of numerous researches. During the disease its quantity progressively diminishes. At the moment of the crisis a veritable discharge occurs. The polyuria is very abundant. The urea, which may have been reduced to 12 or 15 grammes, rises to 30 or 40; the chlorides, which were represented by 1 or even 0.8 gramme, reach 10 and 12 grammes. The modifications in the amount of chlorides have been attributed to the diet. This opinion is inadmissible, for it is contradicted by the abundant discharge at the moment of recovery. It is also known that if chlorides or iodides are adminstered to pneumonia patients, these substances accumulate in the organism and are eliminated only at the time of crisis. Likewise, the phosphates and the sulphates increase when defervescence is produced, but in less notable proportions.

The same is also true with regard to those poisons which are normally excreted by the urine, they being in great part retained in the organism during the disease. During the stationary period the toxicity of the urine progressively diminishes; at the time of crisis it is considerably increased, and reaches, or even exceeds, the normal figure. It should not be concluded from this result that recovery is due to the sudden elimination or to the urotoxic discharge. On the contrary, the reverse is true: it is because the patient has recovered that crisis has appeared. This is proved by the fact that in certain cases the urinary crisis occurs twenty-four hours before, or, what is more demonstrative, after recovery.

Thus the patient, being cured, is capable of rejecting the poisons which impregnate his organism, but to which he had already become insensible. As to the crisis, it is to be considered simply as an exaggeration of normal phenomena. It is established that in a healthy man the elimination of autogenous poisons is not effected in a continuous manner: the urinary secretion varies from one day to another; it follows a tertian, less frequently a quartan type. Then,

even in a normal state of things, accumulations and discharges are constantly produced—that is to say, little crises. It is a particular example of a general law to which we have frequently referred. We have already shown that there is no uniform movement in nature, and that all vital acts are remittent. Starting from this physiological fact, we may regard crisis as a natural phenomenon or an exaggeration of the normal type.

The infectious diseases ending by crisis are not very numerous. Besides pneumonia, which is the type of the kind, we may cite erysipelas, smallpox, and typhus fever; however, crisis is not so clear in all cases, nor is it of constant occurrence.

There is a disease in which crisis occurs in a reverse direction: that is, cholera. In the stationary period the temperature is below the normal; at the moment of recovery it rises above and sometimes reaches a figure quite notably above the normal. Thus, a febrile, reactionary period develops, sometimes attended by grave manifestations, which may impart to the patient a typhoid aspect.

Convalescence.—When the morbid process seems to have been arrested and recovery obtained, the organism is not yet completely restored. There is still a last period termed *convalescence*.

The appetite, which had been suppressed during the disease, reappears, and is often so marked that it is difficult to prevent the patient from overeating. The temperature often falls below the normal; the figures 36.5° and 36° C. are not infrequent, and may be observed for a week or more.

Emaciation appears or increases, this being probably due to the great amount of waste which is eliminated by the different emunctories, notably through the respiratory apparatus and the kidneys. Then, at the end of a few days, the patient grows fat, his weight often exceeding that noted before the commencement of the disease, and at times he becomes slightly obese.

The nervous system having been most affected during the stationary period, therefore returns more slowly to its normal condition. During the first days following recovery, when all the organs are working regularly, the nervous system is still disturbed. The individual is unable to keep on his feet or walk; if an abrupt movement is attempted, dizziness and palpitation are experienced. Now and then a febrile paroxysm occurs, as, for instance, when he happens to read a little too much, or on the occasion of a visit, an emotion, or an act of little importance, such as making his toilet; the thermometer then marks 38° or 38.5° C. These disturbances, which seem to depend simply upon a lack of equilibrium of the centres of thermal

regulation, and not upon an additional infection, are transitory and in no wise disquieting.

The nervous manifestations of convalescence are sometimes much more marked than would be expected in view of the comparatively innocent character of the disease. In this regard nothing is more instructive than influenza. Even after the slight forms which have lasted but a few days, convalescence is very tedious; weakness, asthenia, and incapacity for work may persist for weeks or months.

Finally, some of the symptoms of the stationary period may still reappear. A convalescent from typhoid fever will easily have diarrhoea; a convalescent from a thoracic affection will, upon the slightest cause, cough and have pain in the side.

Evidently the duration of convalescence varies according to the nature, type, and gravity of the disease, and also according to the age or previous condition of the subject. Aged individuals and those who are already weakened require more time to be re-established, and they may often have to go to the country or to a warm climate.

Convalescence may be interrupted by a great number of accidents.

Besides the nervous fevers already referred to, other causes may produce a rise of temperature up to 39° or 40° C. After a day or two the temperature again becomes normal. This is often a process of abortive relapse; the disease, not well extinguished, has recommenced and has been arrested by means of timely medication or the natural defences of the organism.

In other cases a septicæmia is superadded to the primary disease. Some authorities have even maintained that the relapses of typhoid fever should be considered as infections of intestinal origin—i. e., that the alterations of Peyer's patches, by lessening the means of defence, permit the invasion of the economy by the habitual microbes of the alimentary canal.

Febrile paroxysms connected with cutaneous suppurations may also be observed; the alterations of the skin, like those just referred to in the intestine, permit the pus cocci to produce abscesses or boils. At times an infection is produced in other organs; pneumonia occurring during convalescence from any disease may be taken as an example.

Lastly, in certain cases febrile paroxysms occur, which are explained by the aggravation of an antecedent chronic infection. For example, in an individual who has suffered for a more or less considerable period with a torpid (slow) tuberculosis, and then contracts the measles, convalescence does not become duly established after this intercurrent infection; he remains weak and suffering; he has slight fever every night, and emaciates and loses strength; the pulmonary

lesions extend, and finally they either cause death, or, after a certain time, they are arrested and resume their former slow course.

Relapses and Recurrences.—Convalescence may also be interrupted by a relapse.

In certain infectious diseases relapse is the rule. We refer to recurrent typhus, and to a particular form of infectious icterus, improperly called Weil's disease.

Relapse is frequent in typhoid fever, influenza, and broncho-pneumonia; it is rare in uncomplicated pneumonia and exceptional in other diseases. In most cases it is caused by a fault of the physician or of the patient. Alimentation may have been too rapid or too abundant; the patient may have got up too soon, or exposed himself to the cold, and especially to fatigue. It is relatively easy to treat a disease during the stationary period; but at the moment of convalescence the physician is often greatly embarrassed and requires much tact and experience.

Relapse sometimes manifests itself in a slow and progressive manner; more often it appears suddenly, even in the case of typhoid fever. In this disease the temperature reaches 39° or 40° C. on the evening of the first day. In a general way, relapses are less grave and of shorter duration than the primary affection; but there are many exceptions to this rule, and a relapse may be more prolonged, graver, or even fatal.

A distinction has justly been established between relapse and recurrence (*récidive*). Relapse means a new beginning of a disease without a new infection; recurrence is connected with a new infection. In a good many cases the distinction is easy. When a person is attacked with typhoid fever or erysipelas after an interval of fifteen or twenty years, such is evidently a case of recurrence; but when the symptoms reappear at an early period, interpretation becomes extremely difficult. Some individuals, particularly women, have erysipelas every month. Is such a case an example of recurrence or of relapse? It is impossible to answer, since we do not know what period of time is required for the destruction of the germ.

The present tendency is to increase the importance of relapses at the expense of recurrences, and to admit that the microbes remain inactive in the organs and tissues, but ever ready to assume the offensive upon the slightest occasional cause. Indeed, it has even been asserted that in most cases the recurrences of gonorrhœa are but relapses; in fact, the gonococcus persists during an almost indefinite period in the urethra which it has invaded for the first time.

Erysipelas and pneumonia belong to the number of diseases which seem truly capable of frequent *récidives*. Recurrences of measles are

quite common; those of typhoid fever, smallpox, and scarlet fever are very rare. As to syphilis, recurrence is altogether exceptional; most of the cases cited as examples of a second chancre are accounted for by a confusion with tertiary lesions of the genitals, which sometimes simulate a primary lesion.

Passage of Acute Infections to a Chronic Condition.—Although recovery is the normal termination of infectious diseases, there are certain cases in which the evolution is prolonged beyond the usual limits. The disease is then said to have become chronic.

The duration of acute diseases has been arbitrarily fixed at forty days: beyond this term chronicity is supposed to be established.

If the question be considered from a higher standpoint, it will be seen that an essential difference between the two processes is furnished by the study of the evolution.

Acute disease is a morbid process in a state of modification; each day brings about a change which, though often but slightly marked, can nevertheless be recognised by a careful examination. It will then be noted that the organism is reacting—that is, struggling with all its forces to arrest and destroy the morbific cause. It is in revolt against the invader.

In a chronic disease the organism submits to the yoke of the pathogenic agent and seems to have no other ambition than to live with it; it hardly tries to circumscribe its progress; it abandons itself, being incapable of continuing the battle. The reason the condition of the patient is not more quickly reduced is that the invader itself has become less active and aggressive. Thus a tacit agreement is made between the microbe and the organism, and the disease persists, undergoing only extremely slow changes.

Therefore an acute disease is distinguished by a lively, often too energetic, reaction; a chronic disease is characterized by the absence, insufficiency, or slowness of reaction.

At times, however, the organism may for a moment recover its energy. The result is acute attacks, often occurring without any appreciable cause, and at times as the result of exposure to cold, traumatism, or an intercurrent infection. Under such conditions the pathogenic microbe makes a fresh attack, with the result that the organism shakes off its torpidity. This acute spell may be ill directed, undisciplined, and precipitate the morbid evolution and thus rapidly cause death. In other instances, after having given rise to painful symptoms, it will lead the organism to recovery. A rebellious gonorrhœa, for example, has been seen to disappear after a new acute attack. This is a cure of disease through aggravation of disease.

Medicine has attempted to imitate these natural procedures—for example, irritant local applications realize this indication. Koch's tuberculine does not act otherwise; it whips, so to say, the torpid evolution of chronic tuberculosis.

An acute process may become chronic without any notable changes being produced: it stops at a given moment of its course. This may occur at the moment of aggravation as well as at the time of improvement of the disease. The violent manifestations subside, the reactions and pains cease, and in certain cases the symptoms are so slight that the patient believes himself cured. Illustrations abound; they are mostly drawn from cases of nonspecific infections, mainly inflammations of organs—e. g., enteritis, nephritis, and cystitis—which gradually pass into a chronic condition; also various suppurations, commonplace or specific; gonorrhœal urethritis, for instance, is thus transformed and often persists during an entire lifetime, occasioning no disturbance, and unknown even to the patient.

Finally, of the specific infections we must specially mention tuberculosis, which, after an acute attack, may follow a slow evolution.

In order to more closely study the evolution of chronic lesions, let us consider an abscess situated somewhat profoundly. In its development it produces various disturbances. Then, when it is opened to the exterior, the symptoms cease; suppuration, at first very abundant, diminishes progressively. An early recovery may be expected; but at a certain moment the improvement is arrested, and a fistula, giving issue to a sero-purulent liquid, is established. There is no longer any general or local reaction; without any apparent inconvenience the organism supports this lesion, which becomes chronic. However, at the moment when chronicity is established the discharge undergoes some modifications. It loses its freely purulent character; it becomes more serous, more mucous; at the same time, the microbes diminish in number and virulence.

Failure to recover in such instances is often due to the presence of a foreign body, a splinter, or a sequestrum in the focus; or else there is diseased tissue at the bottom of the fistula. When it is possible to intervene and to extirpate or remove this inflammatory thorn, the organism triumphs over the bacteria and the lesion heals. Thus foreign bodies, although absolutely harmless when they are aseptic, maintain an infection which would be cured in their absence; this is a remarkable example of pathogenic association.

In cases of chronic infections, the microbe, although attenuated, is not absolutely inoffensive. It seems even that its feeble pathogenic potency is in great measure due to some protective power exerted by the wall of the morbid focus. Dr. Chauveau has shown that the

pus of a seton which produces no disturbance is virulent; if a particle of it be inoculated in another point of the economy, disturbances are caused. The pus was endured only in its old focus.

In cases of chronic suppuration, fistulæ may from time to time become occluded; the subjacent focus is then filled with pus and increases in volume; it becomes painful and gives rise to fever. After an artificial or natural opening, the lesion resumes its slow and chronic course. In other cases the fistula becomes closed; it appears to be healed, as no symptom is any longer apparent. For months or years the lesion gives rise to no disturbance whatever; then the focus, which seemed extinguished, is again kindled, and a new attack is produced. Such a course is observed especially in osteomyelitis, where a sequestrum may provoke very tardy disturbances appearing at considerable intervals.

The microbe had slumbered for years as an absolutely inoffensive guest; an occasional, often unnoticeable, cause has permitted it to regain a little virulence and give rise to inflammatory reactions.

A similar evolution is sometimes observed after typhoid fever. This disease never passes into a chronic state, but the microbe that has provoked it may become localized at certain points, notably in the bone marrow, and thus call forth a slow inflammation which terminates, after several months, in a focus of osteomyelitis. Bacteriological examination demonstrates the presence of Eberth's bacillus therein. In his case the acute disease ends in a chronic process quite different from what it originally had been.

We can find by no means less interesting examples in the history of *ulcers*. Under this name are designated losses of substance having no tendency toward reparation.

Ulcers result from very varied lesions which, owing to peculiar conditions, have not been able to terminate in recovery.

Let us consider, for example, the varicose ulcer. A slight infection, an abscess, a pustule, a simple abrasion, having induced an infection so mild that no symptom is expressed and the existence of which we admit simply by induction, is the starting point. Reparation is not effected because the tissues are altered; their nutrition is profoundly affected by the varicose condition of the veins; the skin becomes hard, brownish, and sometimes is attacked with eczema. The little lesion sufficed to produce a chronic affection in the suffering tissue.

The same explanation is applicable in ulcerating dermosynovitis. This is a trophic lesion provoked by an ordinary cause or a slight infection, and it develops and persists because nutrition is profoundly disturbed by the nervous lesions. This ulceration is observed especially in ataxics.

The data of clinical experience are confirmed by demonstrating that section of sensory nerves hinders considerably the process of repair. For example, division of the sciatic nerve in a guinea pig is often followed by ulcerations in the foot operated upon. But if care be taken to protect the limb by means of a sort of plaster shoe, infection is prevented and no nutritive disturbance appears.

The same is true of ulcers of mucous membranes. A commonplace lesion, in most cases of an infectious origin, may serve as a starting point for an ulcer of the esophagus, duodenum, and especially the stomach. Ulcer of the stomach develops in hyperchlorhydric dyspeptics; the excess of acid hinders reparation. Filhene has given an experimental demonstration of this pathogenesis. Two rabbits received considerable doses of arsenic subcutaneously: in one of them kept as a control, gastric ulcerations developed; in the other, to which bicarbonate of soda was administered to neutralize the gastric juice, no lesion was produced.

Although the organism plays a very important part in the development of ulcers, we must recognise that the lesion is sometimes dependent upon the nature of the pathogenic agent, its degree of virulence, and the point where it is developed. The ulcerations of tuberculosis, glanders, and syphilis and the phagedenic lesions belong to this group; the influence of the organism, without being absolutely nil, is in these cases considerably reduced.

An acute lesion may pass into a chronic state under a form relatively favourable—namely, *induration*. In such instances the organism was capable of completely destroying the pathogenic agent, but the alterations produced were too profound to admit of perfect reparation. The tissue, instead of returning to its primary condition, is replaced by a newly formed fibrous production. This termination is observed in superficial lesions, in certain abscesses, and in adenopathies, but it is particularly important in deeply situated tissues and organs. In this manner cicatrices are produced which, when located in the mucous membranes, cause deformity and hinder their normal action. When the cicatrices occupy such passages as the esophagus or the urethra, they result in stricture; in the viscera, such as the heart, liver, or kidneys, they produce sclerosis. In these cases the chronic process differs completely from the acute. As we have shown with reference to scleroses, the process of repair remedies the first disturbances, but creates a hindrance to the regular activity of the organs.

The chronic processes, the mechanism of which we have just indicated, undergo no modification or progress slowly, either toward recovery or toward death. In both cases changes ending in one or

the other of these two terminations are produced either in an insidious manner, or else the chronic course is interrupted by an acute attack which leads to recovery or death, as the case may be, or a third alternative leaves the organism in the same condition as before its occurrence.

Death in Infections.—When an acute disease ends in death, the fatal termination may occur abruptly, in an unexpected manner, or slowly and progressively, preceded by more or less prolonged agony. If autopsy is performed, macroscopic or microscopic lesions are sometimes found; in other cases the post-mortem examination gives a negative result. By taking into account the diverse results which may be obtained, the causes of death may be divided into three groups: (1) mechanical disorders or barriers; (2) lesions of an important organ; (3) general infection or intoxication.

As a striking example of the mechanism of *death by a mechanical cause*, we may mention diphtheritic laryngitis. The false membrane developing in the larynx hinders the passage of air and may cause death, partly mechanically, partly through the reflex spasm which it excites. Likewise, a phlegmon taking its origin in certain regions may, by its size or by the œdema surrounding it, mechanically induce a fatal termination.

In these examples death evidently results from the obstacle created by the lesions, since if the false membrane be detached or the circulation of air be re-established through intubation or tracheotomy, or the phlegmon be opened, the disturbances disappear immediately.

The local lesion which may thus endanger life is not, however, the work of a microbe, but is due to a reaction of the organism which seems to fight against itself. If we more closely investigate the succession of the phenomena, we understand that the organism has produced a false membrane or a purulent focus in order to prevent general infection. The lesion thus created was designed to circumscribe the morbid process and to oppose the penetration of microbes or their toxines. However, the organism is not always capable of proportioning its effort to the work required. In a good many instances reaction exceeds the end. A microbe penetrating into the lung induces an acute pulmonary congestion: the vessels dilate in order to facilitate the escape of fluids and cells which will arrest the development of the parasite. But the reactionary phenomena are often too intense, and may give rise to grave symptoms. In other cases, the microbe reaches the surface of the lung and irritates the pleura, which then secretes a fluid, which is often so excessive in amount that evacuation of the exudate becomes necessary.

Lastly, in certain cases reaction is not too strong; it is truly bene-

ficial, but it is produced in particularly delicate localities and on that account may become dangerous. Such, for example, are congestion, œdema, and abscess observed in the brain.

Under these various conditions the organism has endeavoured to remedy the immediate disturbances, but it has mobilized too great a number of cells or given issue to an excessive quantity of liquid.

Therefore, under such circumstances, the necessity of employing therapeutic measures to the organism itself with a view of moderating the morbid reaction and of endeavouring, for example, to check the active congestion, which threatens to give rise to asphyxia by reason of its intensity, is of the greatest importance. At other times, on the contrary, the organism must be aided in its efforts to accomplish that part of its work which it is unable to do alone. Puncture of a pleural collection or the evacuation of a cerebral abscess is not medication against nature, but a complementary method aiding the insufficiency of natural means.

As, on the other hand, morbid reactions may endanger life by their excessive intensity, on the other their insufficiency may be a new cause of disorders. When a microbe develops, it gives rise to the local development of deadly substances which destroy the surrounding cells; the destroyed elements are liquefied and, when possible, thrown out. When the organism fails to remedy the imminent accidents by the various means at its disposal, notably through the accumulation of wandering cells, or if the leucocytes be killed as they arrive at the point of invasion, a more or less complete destruction of the affected tissue will result. Gradually extending, necrobiosis may reach a vessel, and, if the course of the process is rapid, a grave or fatal hemorrhage occurs before a clot is formed. In other cases an important cavity is opened; for instance, the wall of the intestine is perforated.

In these various cases lesions which are apparently sufficient to account for death will be found at the autopsy.

As a result of anatomico-pathological discoveries we have become so accustomed to attach an exaggerated importance to anatomical lesions that we are satisfied when the autopsy reveals a morbid focus in some important organ. Let us take, for example, the case of a child dead of measles. During life a murmur was found at the base of one lung, and, on opening the cadaver, a focus of broncho-pneumonia is, in fact, discovered at that point. The mechanism of death in this instance appears to be easily understood. Yet, on a little reflection, it will be acknowledged that it is hardly possible to attribute the fatal termination to a lesion so small as not to hinder hematosis to any great degree. The same reasoning is applicable to other organs, as well as to those cases in which multiple lesions are

found. In acute miliary tuberculosis, when the tubercles have invaded the serous system only, why has the individual died? Pushing the question further, it must be asked, Why has he succumbed, even when the multiple granules have invaded the viscera? There generally remains sufficient intact parenchyma to assure the function of the organ. Without wishing to abuse examples, we may refer to cerebral softening, which, even when limited, may occasion death, whereas it is possible to experimentally remove the greater portion of the brain without endangering life.

The anatomical lesion is a small matter, and it is not sufficient to explain everything.

It is here that modern science intervenes and rightly proclaims the rôle of toxines secreted in the diseased organs and leads to the admission that death is due to poisoning. This interpretation is confirmed by those cases in which no manifest lesions are revealed by post-mortem examination.

Let us suppose an individual succumbing to anthrax. The blood is disintegrated, dark, and sticky, and the spleen is swollen and the other viscera congested. At times small visceral ecchymoses are met with, and that is all. This is evidently somewhat disappointing. However, on examining a drop of the blood or a particle of the organs under the microscope, innumerable bacilli are observed, and thus some light is thrown on the problem. Here death is attributable to a general infection—Toussaint said it was due to an obstruction of the capillaries by the bacteria. However, this invasion and dissemination of the foreign elements does not seem to be sufficient to explain the fatal termination. It is neither by crowding the vessels nor by abstraction of oxygen or of the materials necessary for cellular renovation that the bacteria have destroyed life. On the contrary, it is by the secretion of soluble substances that the function of the cells has been disturbed.

This interpretation, which may seem contestable as regards anthrax, is the only one admissible in reference to those diseases whose pathogenic agent is localized at a certain point of the organism. In diphtheria, gaseous gangrene, and cholera the microbes do not invade the economy; they remain localized in the skin or confined to the digestive canal. Death can not, therefore, be attributed to any other cause than the soluble substances engendered by the micro-organisms.

It is not enough, however, to say that death is the result of an intoxication; we will endeavour to indicate the mechanism of a fatal termination a little more precisely.

In certain cases lesions are found which of themselves would be sufficient to endanger life. For example, the autopsy reveals degen-

eration of the liver and kidneys, myocarditis, or hemorrhages of the suprarenal capsules; chemical analysis shows the diminution or even the absence of glycogen in the liver; and microscopical examination demonstrates cellular lesions in most of the organs. It may then be asked whether these multiform alterations have not played a part in bringing about the final result, and whether the auto-intoxication resulting from organic insufficiency has not been added to the microbic intoxication. This, however, would tend to again displace the problem, for it is at any rate to be recognised that the cellular lesions are in certain cases too limited to have exerted a marked influence.

We are thus brought to again admit a toxic action. This action, however, is not immediate; the poisons do not kill rapidly, but a certain length of time elapses between the moment of their introduction and the instant when the first responsive manifestations appear. Instead of at once arresting the nutritive activity which essentially characterizes life, and microbic toxines disturb nutrition by adulterating the intercellular medium. Whether the poison itself modifies this medium, or whether the secondary products originating under the influence of the toxine act as a ferment, is a matter of little importance. What is an important fact, however, and one to be kept well in mind, is that even when a fatal dose is at once introduced into a vein the animal succumbs only after the elapse of several hours. This means that a whole series of modifications in nutrition are produced through the influence of the toxine.

We are thus led to consider not the total death, but the individual death of the parts of the organism—i. e., of the cells. It might be supposed that, under the influence of toxines, nutrition is equally perverted in all parts of the organism; but such a conception is hardly admissible. The cells are disturbed according to a fairly determined order—those which perform the highest functions are affected first. Since the nerve cells occupy the highest position, experimentation in accordance with clinical facts shows that it is upon them that the deleterious action of toxines is in most cases exerted. The dynamic state of the nerve cells being thus modified, it is comprehensible that an occasional cause, by producing in them an abnormal excitation, may induce sudden or speedy death. Otherwise, the fatal termination supervenes gradually, as the result of a progressive weakening of metabolism.

In order to admit these different conceptions without reservation, we should be exactly informed as to the functional state of the different parts of the organism at the moment of death. Here is a most difficult question which has not as yet been the subject of experimental studies.

In brief, death as a result of infection is death from intoxication. The microbic poisons accumulate in the organism and hinder or prevent normal cellular life. It is possible that they act by forming combinations with the cellular protoplasm. It is more probable, however, that they affect the cells by adulterating the intercellular medium. The result is a series of functional disturbances inducing death, and at the autopsy no lesion, or almost none, is found even under the microscope. If any lesions are met with they are too small to explain the fatal termination.

If life is prolonged, functional disturbances induce anatomical modifications, and also they secondarily produce important cellular lesions which play an important part in the mechanism of deferred deaths. Here, however, the question is no longer one of infection, but of organic lesions progressing on their own account and deriving no particular character from their origin. We are thus led to say a few words with regard to the evolution of noninfectious diseases.

EVOLUTION OF NONINFECTIOUS DISEASES

It is useless to dwell upon mechanical agents. They do not cause diseases, but they produce lesions only. Popular good sense has long recognised the distinction between wounded and diseased subjects. In the development of wounds we need only study their mode of reparation. Traumatism is sometimes a cause of disease, because it either excites nervous reactions or opens a door, sometimes to intoxication, but generally to infection. It is not necessary to dwell upon these facts, which have already been discussed.

We may also neglect to consider the physical agents, which, as a rule, simply produce lesions or some nervous reaction. The rôle played by them has already been pointed out.

The history of chemical agents—namely, of intoxications—is more important.

Let us first consider *acute intoxications*. In general, a certain time elapses between the moment when the poison is introduced into the organism and the instant when disturbances appear. This is the period of latency, which must not be designated as incubation, since there is no development of a pathogenic agent. Exceptionally, disturbances ensue immediately—for example, when prussic acid is ingested.

The onset may be slow and progressive or abrupt and sudden, and is followed by a stationary *period*, which is generally of quite short duration. As an example we may mention alcoholic intoxication. Drunkenness appears some time after the ingestion of the alcoholic beverage, and its disappearance is rapid and complete. Such is not always the case, however. The absorption of a great amount of alco-

hol may be followed by visceral lesions which are of subsequent and independent development. If the liver is affected, an acute steatosis may be observed, which rapidly causes death, accompanied by manifestations of grave icterus.

Similar remarks are applicable to phosphorus or cantharides poisoning. In both of these instances hepatic or renal lesions occur and continue to develop long after all the toxic substance has been eliminated.

At other times symptoms persist because the poison has facilitated the development of an infection. In mercurial poisoning, a stomatitis or an enteritis, the work of the microbes of the mouth or the intestine, may produce gangrenous and ulcerous lesions in the mucous membranes altered by the mercury. In a similar manner the development of broncho-pneumonia consecutive to carbonic-oxide intoxication must be attributed to the intervention of microbes.

Thus in all acute poisonings we must take into account both the primary and, as a rule, transitory effects produced by the poison, and their more or less deferred consequences, which are due either to visceral lesions resulting from the poisoning or to secondary infection.

Chronic intoxications are far more common and interesting. For years individuals absorb considerable quantities of poison without the least apparent derangement. During this long latent period the morbid phenomena develop insidiously; visceral lesions are produced, and then symptoms appear, either slowly, progressively, or even with an astonishingly abrupt intensity.

The progressive development of morbid events is easily explained by the development and continuous aggravation of the lesions. The sudden and often unexpected appearance of the disturbances is referable to one of the following causes: sudden augmentation of the daily dose of the toxine, suppression of the toxine, or intervention of a new mechanical, physical, chemical, or animate pathogenic agent.

The influence of an increase of the habitual dose is easily understood. A man who is in the habit of drinking to excess will have an attack of intoxication or delirium as a result of indulgence greater than usual. A fresco painter who tolerates his saturnism will have an attack of lead colic after breathing more of the poison than usual—for example, after having scraped a wall painted with white lead.

At first sight it is still surprising to observe disturbances follow the suppression of the daily toxine. The fact is that the poison has become necessary to the regular performance of functions and has been made, as it were, a constituent part of the cellular protoplasm. In other words, it is an indispensable excitant, and if it is lacking disorders become manifest, which disappear as soon as it is again admin-

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istered. Such is the case with the alcoholic and the morphine eater, who are often seized with disquieting symptoms when they are forced to abandon their pernicious habit. As soon, however, as they take a dose of their usual poison, all the disturbances vanish. An idea of the results of a total suppression may be obtained by a consideration of the daily life of an alcoholic. On awakening in the morning, his ideas are not quite clear, and his hands are agitated with a continuous trembling. As soon as he takes a drink, however, the symptoms disappear, intelligence again becomes quite bright and the trembling ceases.

The poison has therefore become indispensable to the regular activity of the organs.

The visceral lesions produced in the course of intoxications, like those developing in the course of infections, often remain latent for a very considerable period. They may give rise to disturbances on the occasion of some intercurrent cause which breaks the unstable state of equilibrium of the organism.

For instance, an alcoholic individual, who seems to be in good health, suffers from a traumatism, a sunstroke, or an infectious disease, when he is at once seized with delirium tremens. The sudden intervention of a new cause provokes the appearance of symptoms. The same is true of an individual affected with plumbism. Lead colic is an acute episode in the course of a chronic intoxication; it occurs, as a rule, as the result of some occasional cause, particularly of an excess in drinking.

The development of visceral lesions is generally caused by intoxications and infections. These lesions, as we have repeatedly stated, develop independently, deriving no particular character from the cause or causes from which they originate.

The symptoms and evolution of a nephritis, a cirrhosis, or a cardiopathy do not differ according to the agent which has occasioned them; on the contrary, everything depends upon the nature and extent of the lesions.

It is readily understood that a profound but localized alteration is far better borne than a superficial but diffused one. Likewise, symptoms are less marked when the interstitial tissue is affected than when the glandular cells are attacked. It is true that the organs comprise a much greater number of cells than is necessary for the continuation of life. From 40 to 50 per cent of the glandular tissues may be suppressed with impunity; one third of the liver may be removed, one kidney extirpated, or one lung excised, without any great disturbance. With certain glands, even very important ones like the pancreas, a very small part suffices for the regular performance of their functions.

These remarks perfectly explain the frequency of latent affections.

A visceral lesion may run its course silently for months or years without expressing itself by any symptom. The organic lesion will be discovered perchance. On auscultating the heart the physician may find an aortic insufficiency until then unsuspected, or, on examining the urine, he finds sugar or albumen, while no disorder whatever made him suspect the existence of diabetes or nephritis.

Notwithstanding the absence of disorders, these lesions constitute a permanent danger, for sudden or unexpected death is often the consequence of such latent conditions.

In certain cases symptoms appear progressively or abruptly, being excited by some intercurrent and often very slight cause. The organism is in such a state of unstable equilibrium, however, that disturbances may appear on the slightest occasion. Thus, a hepatic cirrhosis may remain absolutely latent; then, in consequence of a cold, ascites rapidly develops, and from that moment all the manifestations of the affection are displayed.

The symptoms produced in the course of a permanent affection are often transitory; they cease and subsequently reappear, although the lesion persists. We are thus led to say a few words in reference to intermittence in diseases.

Without again referring at length to infections, we shall first recall the example of malaria. The paroxysms occur periodically, leaving the condition of health intact in the intervals. It is admitted in this instance that intermittence is explained by the life cycle of the parasite. However, in visceral suppurations the fever may also assume the same character. While the cause acts continuously, the organism acts only in an intermittent manner. The same fact is observed (and its interpretation then seems much easier) when there is excitation of a mucous membrane. Thus, in spasmodic laryngitis or croup, the glottic obstacle, though permanent, gives rise only to attacks of suffocation of a paroxysmal character. Although the lesion remains the same, and does not vary from one moment to another, it excites spasms only at intervals. Then, after an effort, perhaps as the result of exhaustion, the affection resumes a milder course. It may be remarked that physiology has prepared us to accept these results. For the production of a phenomenon, a series or a summation of excitations is often required; reciprocally, the excitation persisting, the effect may cease. An energetic current applied to the pneumogastric nerve arrests the heart, but only for a moment, since, despite the persistence of the stimulant, the beating recommences.

Similar phenomena are observed under a great number of circumstances. Even traumatic lesions are not exceptions. The pain felt in old cicatrices on seasonal or barometric variations pre-

sents a periodicity which is explained by the influence of cosmic variations.

The mechanism of periodicity in chronic affections is a subject of special interest. This mechanism may easily be explained by one of the following two processes, as the case may be: At times there is a slow accumulation of toxic substances and the paroxysm breaks out when the toxines become too abundant; at other times there is a circulatory hindrance, and nutrition, although sufficient in the state of rest, is unable to supply the needs of the organ during the period of activity.

In the former case, the paroxysm may be looked upon as a sort of discharge calculated to neutralize, eliminate, or modify the toxic substances. There is a growing tendency to attribute to auto-intoxication an important rôle in the genesis of paroxysmal manifestations occurring in the course of a neurosis. The fit of epilepsy has been explained in this manner. Whatever may be the value of this hypothesis, it is undoubtedly true that the patient feels better after a crisis: he finds himself relieved by a sort of salutary discharge. The same remark may also be applied to the intermittent manifestations which occur in the course of diatheses. An asthmatic and particularly a gouty paroxysm are prepared by modifications of nutrition, which is subsequently improved in a notable degree. The subject experiences a feeling of well-being. Then, little by little, the disturbances slowly and insidiously return, until they end in a new attack.

The second mechanism above referred to is much better known. It is best exemplified by arteriosclerosis. In this affection, the arteries having lost their elasticity, circulation is unsatisfactory: as long as the organs are at rest, reparation is sufficient; as soon, however, as they become active, disorders become apparent. In this manner a syndrome is produced which can be studied in animals as well as in man—i. e., *intermittent claudication* (limping). Whenever the subject walks for some time the insufficiency of arterial circulation hinders the activity of the muscles and gives rise to limping.

What is easily observed in the limbs is equally produced in the viscera. According to the felicitous expression of Grasset, an intermittent claudication of the organs exists. Visceral disturbances become manifest as soon as a more active circulation becomes necessary. A good many causes may therefore give rise to this phenomenon. As a clear illustration, we may take sclerosis of the coronary arteries. Although the circulation has become very defective, no disturbance is produced; then, all of a sudden, a paroxysm of angina pectoris occurs which seems to appear spontaneously and without any apparent cause. In reality, it is due to some gastrointestinal, pulmonary, cardiac, or

nervous disorder. A too hearty meal, difficult digestion, exposure to wind, overexertion, a strong moral impression have demanded of the heart an increase in work. This organ, which accommodated itself to the ischæmia produced by the sclerosis of the coronaries as long as its activity was moderate, no longer receives a sufficient amount of blood under the new conditions. Therefore the first manifestation of a chronic, slow, and progressive process appears abruptly. At the end of a few minutes the symptoms subside, and the individual resumes the appearance of good health until the moment when a new attack occurs. In proportion as the attacks are repeated, however, the minutest causes suffice to provoke their return. A time arrives when the attacks seem to be produced spontaneously; the occasional cause is too slight to be recognised.

The same thing may be repeated with regard to many other manifestations. The attacks of asystole, despite the persistence of the lesion, are also intermittent; they appear on the occasion of some intermittent cause, which will become slighter in proportion as the accidents are aggravated, and, in the end, will pass unnoticed; the paroxysm will possess the appearances of spontaneity.

The same remarks are applicable to other organs and to various apparatus—lung, liver, kidney, and the nervous system.

LATENT DISEASES.—If the accessory cause which explains the development of periodical accidents is lacking, the disease may remain latent.

Diseases, even those that are acute, are sometimes unexpressed by any disturbance. Among the infectious diseases, we shall only mention typhoid fever and pneumonia. There are cases of typhoid fever in which the symptoms are so feebly marked that the subject continues to attend to his business. This is the form which has been well studied under the name *walking typhoid fever*. While generally innocent, this form does, however, occasionally expose the subject to terrible complications, and may end in rapid death by perforation of the diseased intestine.

Pneumonia is quite frequently latent in the aged. No reaction is produced; the individual gets up, leads the same existence as on the preceding days; then he suddenly becomes ill and succumbs in a few minutes. The autopsy shows gray hepatization of one of the lungs, and the observer is astonished that lesions so strongly marked should have developed without giving rise to the slightest symptom.

Among latent affections we may cite a goodly number of cases of pericarditis, pleurisy, and even acute meningitis. Consecutively to an otitis or a sinusitis, diffuse suppurations may invade the meninges without any reaction being produced, not even slight headache.

Lastly, it must also be remembered that chronic affections of the organs, such as cirrhoses of the liver, nephrites, valvular lesions, and particularly aortic insufficiency, spinal and cerebral affections, gastric ulcer, and sometimes cancer, may remain latent for a great length of time, and they may subsequently produce rapid disturbances or even cause sudden death. They may finally give rise to no manifestation at all. They are revelations of the autopsy.

The evolution of a disease may be modified by various superadded phenomena and by intercurrent complications. In certain instances the occurrence of a complication causes the primary phenomena to disappear. Nervous affections and parasitic diseases of the skin have been seen to stop for a time on the appearance of some acute infection. Lastly, in certain instances, an existing manifestation suddenly vanishes when a similar phenomenon develops at another point. This is known as metastasis.

Metastasis.—Metastasis is the transportation of a morbid process from one point of the organism to another. In order for metastasis to exist, the transportation must be complete—viz., the primary lesion must disappear.

According to this definition, the so-called metastatic abscesses are very improperly so named. In this case there is not a disappearance of the initial process, but a generalization of an infection. Nor are the cancer metastases to be admitted. When an epithelioma of the intestine is followed by the development of a similar neoplasm in the liver, it is a case of extension through embolism.

Thus defined, metastases are quite rare. A few examples have been observed in infections—e. g., the urethral discharge often disappears when a gonorrhœal orchitis supervenes. A better example is furnished by the history of rheumatism: when cerebral manifestations appear, the swelling of the articulations diminishes and the pains often disappear with astonishing rapidity; there is a transportation of the fluxion which leaves the articulations to invade the nervous centres. In fact, the congestive and fluxionary phenomena are the most easily displaced. The knowledge of these facts has led to an important therapeutic method—i. e., *revulsion*. When cupping is practised upon the thorax, pulmonary congestion diminishes; when an irritation is provoked in the intestine, the encephalonic or meningeal congestion is diverted. From this point of view calomel gives excellent results. By creating a new congestive process, it is possible to cause the older one to disappear—i. e., to provoke a metastasis.

If we consider the diathetic affections, or, to speak more exactly, if we consider arthritism, we find well-known facts entering into this

group. Between certain morbid manifestations a perfect balance exists, and the ancient physicians have laid much stress upon the diseases which it is frequently dangerous to cure. Facts of this kind are to-day regarded as doubtful, perhaps on account of their being difficult of interpretation. It seems certain, however, that the disappearance of an eczema may be followed by an attack of asthma, and a very curious balance exists between certain skin diseases and various internal manifestations—e. g., hemicrania, enteritis, etc.

Gout may also alternate with various diathetic disorders. Its study also furnishes an excellent illustration of metastasis. An individual is seized with a very painful paroxysm; the big toe, much swollen and red, causes intense suffering. In order to mitigate the pain, he plunges his foot in cold water; relief is at first produced, but soon visceral symptoms appear, involving the heart, the brain, or the stomach—symptoms which are often very grave and sometimes fatal. It is then said that gout has retroceded or ascended. The idea of this misplacement may appear odd; but it must be recognised that to-day, just as in the past, no satisfactory explanation can be given. Several observations recorded as examples of retroceded gout are undoubtedly referable to gastritis or to degeneration of the myocardium, and especially to uræmia. Nevertheless a few facts remain that can not be thus explained. For want of a better explanation, we shall consider them as belonging to the group of metastases.

Recovery.—Whatever may be the disease under consideration, recovery may take place gradually or abruptly. In the latter case a true crisis is produced; the symptoms yield at once; the previously disturbed organic functions are re-established, or they may even be augmented and exceed physiological limits. Thus in a great number of diseases the urinary secretion diminishes. At the moment of recovery there occurs a urinary discharge similar to that which we have noted in infections: a transitory polyuria appears during one or several days. This urinary crisis is of very common occurrence after intoxications, painful affections, and in the course of affections of the organs—e. g., liver, kidney, and heart.

The same variations may be produced in the temperature. If hyperpyrexia has existed during the disease there will be hypothermia at the time of recovery, and *vice versa*. In a great number of intoxications, as in certain infections, such as cholera, for example, the grave events are accompanied by a rectal temperature as low as 35.5° or 36° C. Subsequently, at the time of recovery, a reaction is produced and the thermometer reaches 39° or 40° C.

In the case of a transitory disease or affection, recovery of health may seem complete and the cure perfect.

As regards chronic affections, the morbid symptoms may also decline, and, on a superficial examination, recovery may seem to be established and all the lesions repaired. In reality such is not the case.

Every morbid manifestation lasting for some little time brings in its train irreparable lesions. The disorders cease because a series of modifications which assure compensation have been produced. There first occurs disappearance of altered elements, which are replaced by connective tissue—the cicatricial tissue which always comes to fill the vacant space created by the destruction of differentiated elements. The organism possesses such an overabundance of cells in its glands as well as in its most highly organized parts, such as the nervous centres, that it does not feel the loss of a few of them. On the other hand, the healthy supplement the diseased parts, and compensating hypertrophies and hyperplasias are thus produced. This is a mechanism which we have studied at length in connection with morbid sympathies (page 328). The cardiac hypertrophy that assures the compensation of a valvular lesion or contributes to the re-establishment of the activity of a diseased organ, such as the kidney or lung; the hypertrophy of the bladder, which overcomes the difficulty of micturition in cases of urethral stricture; the hyperplasia of the liver or kidney, which furnishes new elements to replace those which have been destroyed, for some time maintain an almost normal state of health. This re-establishment, however, is but apparent. Sooner or later a functional insufficiency appears, which brings fresh disorders in its train.

Absolute cure is not possible save in traumatism. In nontraumatic cases the functional disturbances may recede and disappear; the organism then seems to return to a state of health as perfect as before the disease. In reality, however, the pathogenic cause, whether toxic or infectious, has imposed a lasting modification upon the nutrition of the subject. This modification, which, as we have repeatedly stated, explains recovery, will carry the economy out of the physiological channel. So that after each morbid effect there still persist some changes which are often too small to be noticed, but which, if the pathogenic causes be repeated, may, by summation, result in more or less marked lesions, new disturbances, organic affections, or finally in death.

Death.—Death may occur in two different ways: progressively, as is most frequently the case, or suddenly. Two varieties of sudden death are to be distinguished. At times the termination is foreseen. The physician can diagnosticate a disease or a lesion recognised to be capable of killing suddenly. For example, a person known to have

aortic insufficiency may live for ten, twenty, or thirty years without suffering at all from his lesion; but he is liable to succumb at any moment.

Facts of this kind are not legally considered as cases of sudden death. In legal medicine this distinction is reserved for unforeseen death, attacking individuals in apparently good health; for it is demonstrated that a really healthy individual is not exposed to sudden death. Traumatism excepted, it may be affirmed that every individual succumbing suddenly was affected with a lesion which was until that moment latent.

It is said, and constantly repeated, that sudden death is generally due to rupture of an aneurism, or to cerebral congestion. This is an error. According to the statistics of the Paris morgue, rupture of an aneurism is not encountered even in the proportion of 4 per 1,000. As regards cerebral congestion, Professor Brouardel declares he has never seen it in cases of sudden death.

What is most frequently found is degeneration of the myocardium, aortic insufficiency, interstitial nephritis, gastric ulcer, and sometimes pleurisy or embolism. Finally, in some cases tuberculous meningitis, and especially suppurating meningitis induced by a purulent coryza or otitis, are observed.

Since the time of Bichat, classical works repeat that death is effected through the lungs, heart, or brain. It is quite evident that death through the brain can no longer be admitted to-day; it should be said that death occurs rather through the medulla. Thus modified, the conception is still inexact. In fact, we must rise to a higher idea and look for the mechanism of death, not in an apparatus, but in a general disturbance, in some modification affecting the function of the cells. We are thus brought to consider death as connected with an arrest of cellular nutrition.

In certain instances this arrest of nutrition may occur under the influence of violent excitation, as is the case in nervous shock. The exchanges between the morphological elements and the surrounding medium are suppressed; there is a retention of noxious products in the cells and lack of renovation of the humoral medium.

In most cases death occurs because waste substances accumulate in the humours and arrest the nutritive exchanges. This is what notably occurs when lesions exist in the liver and the kidneys. Hence, when death is spoken of as occurring through these organs, it is meant that there has been an auto-intoxication of the organism as the result of their disorders. Similarly, when there is an arrest of the heart—namely, syncope—or suppression of the pulmonary emunctory —namely, asphyxia—death results from a lack of organic depuration.

The blood during cardiac arrest no longer carries to the various cells the substances necessary for their nourishment, and is therefore unable to rid them of useless materials. In asphyxia the absorption of oxygen and the rejection of carbonic acid do not take place, and this also results in intoxication.

Therefore, in thus attempting to penetrate the mechanism of death, we reach the conclusion that the fatal termination can not be explained by the lesion or the suppression of an organ. Those who have upheld this hypothesis have considered the apparent phenomenon; they have given a formula applicable only to higher individuals; they have proposed a restricted definition for a general manifestation. The suppression of a function can not characterize a process which is observed when that function no longer exists.

Death, like life, can not be understood except when all series of beings are taken into consideration. Its definition is therefore to be looked for in the disturbances, not of an apparatus, but of all the cells. In other words, in the higher forms of life we must consider two orders of phenomena: (1) a suppression of functions which does not constitute death, but leads to it if the disturbance persists; and (2) an arrest of nutrition which indicates the true cessation of life. The suppression of cardiac pulsations, for instance, is not synonymous with death, for if they recommence, the individual revives. The same is true as regards suppression of the pulmonary function. Puncture of the medulla itself is not necessarily fatal, since artificial respiration may maintain life. All these lesions and disturbances only prepare the fatal termination.

Now, with reference to nutrition, we have shown that cellular nutrition and the organs concerned therein should be considered separately. Cellular nutrition is the general phenomenon essentially characterizing life; its suppression characterizes death. If we consider the unicellular beings, we readily understand that nutrition will stop under two quite different conditions. Sometimes the cell will lose its aptitude to derive from the liquid medium wherein it lives the materials necessary for its incessant renovation, and to throw out those that have become useless or harmful. These conditions are realized under the influence of certain too violent excitations or of certain lesions produced by mechanical, physical, or chemical agents. At other times the medium itself becomes unfit for maintaining life, on account of the nutritive elements having been exhausted or the cellular wastes having accumulated.

These extremely simple facts will permit us to explain the mechanism of death in higher beings. In fact, we find the same two conditions.

A shock or violent excitation may cause arrest of nutrition; but it is readily understood that the pathogenic cause can hardly act at once upon all the cells of the economy. This hypothesis, which might be maintained with regard to some poisons, is hardly probable. In most cases the arrest of general nutrition is produced through the nervous system. Let us take, for example, a violent traumatism. In the case of a unicellular being it inhibits directly the nutritive activity of its protoplasm; in the case of a higher organism it produces an excitation of the nervous terminations which gives rise by reflex action to the morbid state already studied at length under the name of nervous shock. The mechanism is more complex in the latter case, but it is essentially the same. It also intervenes in internal traumatisms —for example, when a pulmonary embolism, a cerebral embolism, or hemorrhage cause sudden or speedy death.

Toxic substances also kill by arresting cellular nutrition. Sometimes they form stable combinations with the protoplasm; sometimes they seem to act by transmitting to it a sort of molecular vibration. In considering a unicellular being, it is easy to conceive the mechanism of death in both cases. In individuals of a higher rank, however, it would be necessary to admit that all the cells are simultaneously killed by the poison—a thing that can never be realized. Certain highly organized cells, notably the nerve cells, are the first to die. If the being succumbs, it is because disorders have been secondarily produced in the humoral medium—i. e., in the plasma in which the cells are immersed. The phenomena thus become more complex, a fact that is due to the greater complexity of the organism.

In order to understand the mechanism of death we must recall what has been stated in connection with nutrition.

The higher beings are provided with an internal medium whose constitution must remain fixed and invariable. Numerous organs work to this end. If one of them should stop working, if others should be unable to take its place, death will be the consequence.

Let us see the principal cases which may be encountered.

1. The materials of renovation are no longer furnished to the blood, because the subject is submitted to inanition, or because the digestive canal has become incapable of transforming or absorbing food; death ensues because the first act of nutrition—assimilation— no longer takes place.

2. The result is similar when the requisite amount of oxygen is not furnished to the cells, either because the red blood corpuscles are not sufficiently numerous, or else they are no longer able to fix this gas, as occurs in carbonic-oxide poisoning.

3. In case of arrest of the circulation, the suppression of cardiac

activity causes death because cellular renovation is no longer effected, and the blood, which serves at the same time as a way of excretion, ceases to throw out the useless substances.

4. The situation is quite similar when respiration is arrested: the cells succumb because the gaseous exchanges are suppressed; oxygen no longer arrives and carbonic acid is no longer exhaled.

5. Lastly, the arrest of nutrition may result from lack of depuration consecutive to alterations of the emunctories. The products of disassimilation are no longer rejected; they saturate the medium and prevent diffusion of harmful substances out of the cell. The lesions of the liver, kidney, and highly vascular glands kill by this mechanism; they arrest nutrition by virtue of the auto-intoxication which they produce.

In brief, if the proceedings called into play are multiple, the final result is always the same. In vegetables as well as in animals, in unicellular beings as well as in those placed at the top of the scale, death is always produced through the same mechanism.

Therefore, modifying the usual formula, we shall say: Death is the result of an arrest of cellular nutrition, either because the protoplasm becomes incapable of carrying out the double movement of assimilation and disassimilation, or because the medium in which the cells are immersed or in contact undergoes modifications rendering exchanges impossible.

The arrest of nutrition is a general phenomenon applicable to all beings. In all it is due to either of the two mechanisms above indicated. In the higher organisms, however, it occurs under conditions more and more complex in proportion to the growing complexity of the apparatus concerned in assuring the activity of the protoplasm and the renovation of the organic medium.

CHAPTER XXI

EXAMINATION OF THE SICK

General appearance of the patient—Posture—Facies—Corporeal deformities—Examination of the integuments—Systematic examination of the various apparatus—General rules for the examination of the circulatory and respiratory organs, the digestive canal, liver, spleen, pancreas, peritoneum, urinary and genital organs, and the nervous system.

THE examination of patients may be made in several ways. It is customary, however, to follow an almost identical course in all cases. The external appearance, the facies, and posture of the patient are first noted; at the same time some questions are asked him as to pain and other disturbances from which he may be suffering. The first impressions thus obtained give an idea of the nature of the disease and serve as a guide to exploration. The hereditary and personal antecedents and present symptoms of the patient must then successively be considered.

As already stated, the first question asked of the patient is intended to locate the seat of his pain. In most instances the phenomena of pain lead us to an immediate recognition of the parts affected. Spontaneous pain and that which is excited by touch or movement, and which may therefore be located with greater precision, are of unquestionable semeiological value. It is well to remember, however, that the investigation of the phenomena of pain may also lead to error. For instance, an individual complains of pain in the stomach and frequent vomiting. Gastralgia is at once thought of, and the stomach is treated with negative result. Here failure to relieve the patient is due to the fact that the gastric symptoms were those of ataxia. At other times patients with some spinal disease complain merely of pains irradiating in the limbs or located in one or several of the joints; these pains are too hastily referred to rheumatism, and sodium salicylate or antipyrine are prescribed without effect.

In this connection the morbid sympathies which unite the heart and the lungs are pre-eminently instructive. Physicians are often

consulted by patients complaining of palpitation of the heart. In fact, the pulse is found to be quick, beating from 100 to 120 per minute. Bromide is prescribed with no benefit, and digitalis causes aggravation of the symptoms. Here nonsuccess is due to the fact that these so-called cardiac patients are in reality pulmonary consumptives; they are subjects of lung lesions which are unattended by any lung symptoms, but which could readily be discovered by means of auscultation. On the other hand, many young women complaining of slight but persistent cough, complicated at times by hemoptysis, are treated as consumptives, dosed with cod-liver oil and creosote, and repeatedly cauterized at the apex of their thoraxes, and yet the respiratory apparatus is intact or but secondarily disturbed. The initial lesion is seated in the heart: it is simply a case of mitral stenosis.

These few examples sufficiently prove the necessity of always examining all the organs in a systematic manner. This is the only means of avoiding such gross errors as have just been referred to.

General Appearance of Patients

Before entering upon a methodical examination of the organs, however, it is necessary to exactly observe the patient's attitude, facies, and general appearance. While ancient physicians knew nothing of percussion, auscultation, or bacteriology, and the methods of exploration employed by them were rudimentary, they have nevertheless left us certain precepts which it would be an error to ignore. At the present day too much is made of scientific procedures.

Attitude, Decubitus.—In case an individual is so seriously affected as to be compelled to lie in bed, his posture must first be noted.

In the first place, there is the horizontal posture upon the back. As a rule, this is the position assumed by individuals in suffering, and by those who are exhausted or have lost consciousness. The same position is taken by those attacked with hemiplegia, although somewhat modified by the fact that the paralyzed side, being less strong than the other, shrinks, as it were, and the healthy side appears to be prominent. In a case of cerebral anæmia the head is low; in that of congestion the head is raised high and supported by pillows; the relief produced by this position is so considerable that even patients in a semicomatose state constantly ask to have their heads elevated.

Another variety of horizontal decubitus is the lateral, which is frequently observed in cases of thoracic affections.

When an individual has pain in the side not connected with any alteration of subjacent organs—in other words, when he suffers, for instance, from neuralgia, pleurodynia, or muscular rupture—he lies upon the affected side. The compression thus produced diminishes

the pain; a feeling of relief is experienced by pressing the hand upon the affected part or by compressing it against the bed.

The phenomena are more complex in cases of acute affections of the respiratory passages. At the outset the patient lies mostly upon the healthy side; later on he lies upon the diseased side, in order to breathe more freely with the intact half of the chest. In case of pleurisy it is altogether impossible for the patient to lie upon the healthy side, for the effusion, obeying the laws of gravity, compresses the mediastinum and presses against the intact side, thus preventing respiratory movements.

In cardiac diseases the victims lie upon the right side. This is an exaggeration, as it were, of a normal phenomenon; even in good health it is more or less uncomfortable to lie upon the left side. At a more advanced stage the sufferer assumes an altogether peculiar position: he sits with his head and shoulders supported by pillows; the legs are dependent, while his arms are kept in a motionless position with a view to furnish a point of support to the auxiliary muscles of respiration.

In case of abdominal superficial pain, the sufferer will likewise try to exert pressure upon the abdomen: sometimes he will lie extended upon his back with the thighs and legs bent, the hands widely opened and pressing upon the abdomen; at other times he will simply lie upon his abdomen. If the pain is very intense there will be agitation and frequent change of position. In some instances the decubitus is quite peculiar and might be called semilunar incurvation. The patient is rolled upon himself; the vertebral column describes a half circle, and the thighs are flexed upon the pelvis. This position is observed in cases of peritonitis, and in hepatic or renal colic. It is also well to be acquainted with the odd positions assumed by those suffering from gastric ulcers. At the time of a paroxysm the patient instinctively assumes a posture calculated to avoid contact of the food with the diseased walls. If the anterior surface is diseased, he lies upon his back; if the posterior surface is the site of ulceration, he lies upon his abdomen; he lies upon his right or left side according as the ulcer is situated upon the left or right side. The importance of these various attitudes is readily understood with reference to the diagnosis of the site occupied by the gastric lesion.

Finally, there is another posture which is frequently observed in tubercular meningitis: the child lies upon one side, with the legs strongly flexed upon the thighs.

The Facies of Patients.—Next to the posture, the facies of the patient must be noted. A great number of nervous or mental derangements impart to the face an altogether peculiar expression. In

some instances the peculiar appearance results from paralysis of certain muscles—e. g., the immobility of the eyes in external ophthalmoplegia, the crying countenance in labio-glosso-laryngeal paralysis. In other cases the features remain motionless—e. g., in paralysis agitans; or the integument loses its property of contractility, as is exemplified by the marblelike countenance in sclerodermia and by the lunar facies of myxœdema subjects. In other instances parts become unduly developed, as occurs in acromegalia, or they become asymmetrical. Paralyses of the seventh pair, whether central or peripheral, associated with or without hemiplegia; paralyses of the motor oculi, conjugate deviation of the head and eyes, glosso-labial hemispasm of hysterical subjects, the facial trophoneurosis of Romberg, all give rise to absolutely characteristic deformities.

Likewise, in the course of various neuroses the facies offers some peculiar characters. The staring and ecstatic expression of hysterical patients, the stupefied aspect of an epileptic after an attack, the particular countenance imparted by the exophthalmia of Graves's disease, represent as many well-known examples.

The expression of the physiognomy is of great importance in the diagnosis of cerebral diseases. According to the type of mental derangement, the countenance is calm or agitated, indifferent or preoccupied, depressed or inspired. The contracted visage of the lypemaniac, the satisfied countenance of the general paralytic, and the wandering look and trembling lips of the alcoholic are also matters of common observation.

We can not undertake to describe all the different appearances which may be observed in various diseases. We shall recall the adenoidian facies, characterized by a stupid expression, transversely flattened nose, half-open mouth, and effaced naso-genian folds; the facies of drinkers, characterized by a nose increased in size and covered with small veins; the mitral facies, with bluish lips, cyanosed cheeks, and puffed skin; the aortic facies, intensely pale; and the Brightic facies, swollen and whitish, etc.

We must dwell somewhat longer upon the modifications, and particularly the dyspnœa produced by thoracic diseases, and upon abdominal affections.

Three types of dyspnoic facies have been distinguished. One is due to defective inspiration. For example, there may be in the larynx some trouble caused by a foreign body or a diphtheritic pseudo-membrane, in which case the patient remains sitting with the neck strained, eyes protruded, nostrils dilated, and the face very pale. In the young each inspiration produces a visible depression above the sternal notch and along the border of the false ribs: this is the

suprasternal and infrasternal retraction caused by the action of atmospheric pressure.

In case of expiratory disturbance the appearance is entirely different. The face is flushed, puffed, and bluish; the cervical veins are much distended; the eyes are motionless, half closed, and tears flow from the eyelids. This is the asphyxial facies.

The third type occurs in consumptives. Its characteristics are, as every one knows, emaciated figure, protruding and red cheeks, fine nose with a jerking respiration, difficult speech, and often extinguished voice.

Of the abdominal facies several varieties are admitted.

In the first place there is the *facies grippé*, which is met with in grave lesions, in peritonitis, intestinal occlusion, and at times in hepatic and renal colic. The striking feature is the considerable diminution in the size of the features; the face appears to be shrunken and diminished; the nose is thin, elongated; the muscular fibres have retracted, and this renders the osseous prominences more appreciable. The skin is pale and often covered with cold sweat; the integument loses its tenderness and elasticity; hence, the folds made in it persist for quite some time.

In children suffering from digestive disorders and marasmus the features are drawn, the furrows deepened, the neck hollow and emaciated. The facial expression recalls that of a little old man.

A third type is represented by the *cholera facies*. The integument is violet, the nails dark, the lips blue, the eyes sunken in their orbits; the extremities, nose, and lips feel cold to the touch, and even the breath is cold. This special type, realized to its highest degree in cholera, is encountered in a great number of other diseased conditions accompanied by choleriform manifestations; it may almost be designated as the facies of agony.

Three more particular facies may be admitted: the syncopal, the apoplectic, and the agonal facies.

Syncope is characterized by an abrupt arrest of the heart; the individual becomes completely pale, respiration is suspended and the pulse imperceptible. In case of apoplexy the patient is motionless and lies upon the back; all the functions are in abeyance; breathing and circulation alone persist. Even these, however, are profoundly modified; the breathing especially is noisy and often stertorous. Finally, when agony arrives, as it does in most acute or chronic diseases, the cerebral functions are gradually suspended; respiration is painful and slow, the skin retracts, the nose is tapering, the eyes are dull, half closed, and glassy. Then breathing is gradually arrested; after a few minutes of apnœa it is resumed, but again stops;

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finally, a last inspiration takes place, and often the body is shaken by a slight spasm; the pupils suddenly dilate and the extremities are in complete relaxation. This is death.

Corporeal Deformities.—In order to complete the study of the external habitus of the patient, corporeal deformities must be looked for, the existence of which is often of very great semeiological importance.

The patient should be examined, when possible, both in the reclining and upright position. The appearance of external forms may be noted in these two positions; moreover, it is well to instruct the patient to take a few steps, which may cause certain symptoms to become more manifest.

Deformities may be general or partial.

The general deformities are, as a rule, referable to alterations of the skeleton. Rickets and, less frequently, osteomalacia produce deformities which may be very extensive. The appearance of a rachitic is a familiar one: the child's stature remains short, while the head is voluminous, with tardily closed fontanelles, the spine is incurved, the ribs are deviated so as to form two prominences, the pelvis is deformed, the limbs are curved, and the epiphyses too voluminous.

Furthermore, it is well to know that even a partial lesion, provided it is profound, may cause secondary deformities modifying the entire architecture of the body. Such is the case with Pott's disease.

Finally, general deformities may be produced by muscular atrophies, provided the latter be extensive and involve most of the muscular system.

Partial deformities must be looked for successively in the head, trunk, abdomen, and limbs. In all regions deformities may depend upon some lesion of the skin or subcutaneous cellular tissue (dermatitis, cicatricial retractions, keloids, tumours, abscesses, œdema, etc.), or the vessels (aneurism, varices), or the muscles, skeleton, and, in the case of the head and trunk, of subjacent organs. In the head, deformities may affect the cranium; they are referable to the epoch when the sutures, not having yet been effected, the lesions of the brain and meninges induce deformities of the skull, which moulds itself upon subjacent parts. It will suffice to mention hydrocephalus as an example.

Of the main deformities affecting the face may be cited trophoneurosis, the deviations due to paralyses or contractures of the muscles supplied by the seventh pair, fluxion and swelling of the parotids (parotiditis and mumps), and the protrusions caused by suppuration or tumours in more deeply seated parts, especially the sinuses of the face.

Thoracic deformities, apart from those produced by rickets, are

due to affections of the lungs, and, less frequently, of the heart. At times they are bilateral and symmetrical, as in the case of pulmonary emphysema; at other times they are limited to one half of the chest, as occurs in pleurisy, pneumothorax, pleuro-pulmonary cancer, and tumours of the mediastinum. The diseased side is expanded and remains so even during expiration, which thus exaggerates the differences. In case of chronic pleurisy, retraction of the organized exudate consecutively produces flattening of the affected side.

There are also partial protrusions due to the presence of aneurism, abscess, or empyema bulging exteriorly under the form of a large tumour, which sometimes presents pulsations (pulsatile empyema).

Alterations of the heart are less frequently productive of deformities. In case of considerable hypertrophy or pericarditis with profuse effusion prominence of the præcordial region is observed.

Likewise the deformities of the abdomen may be general or partial. The abdomen is distended and increased in size in case of ascites, tympanites, and acute or chronic peritonitis. In other instances a region presents an anomalous prominence—e. g., considerable hypertrophies of the liver or spleen are expressed by a tumefaction of the hypochondrium, which is quite notable when the patient is standing. The lower abdominal organs very frequently give rise to deformities: a distended bladder, a uterus that is gravid or full of fibromata, and ovarian cysts are the most important causes.

Examination of the external anatomy of the different members of the body, and particularly the extremities, should never be neglected. In fact, they may present numerous trophic disorders, many of which are of certain semeiological value. Some deformities are connected with nodular rheumatism, while others are due to chronic gout. There is a morbid state characterized by considerable hypertrophy of the extremities—namely, acromegalia. Finally, there may be observed upon the third phalanges of the fingers the so-called nodes of Heberden; the so-called nodes of Bouchard upon the second phalanges, and connected with nutritional disturbances, particularly with dilatation of the stomach; the spatular fingers met with in children suffering from congenital cyanosis; the Hippocratic fingers, characteristic of tuberculosis; and the pneumic arthropathies of Marie, which occur when pulmonary respiration is greatly embarrassed.

The study of deformities of the hands will be completed by looking for a manifestation described by Landouzy under the name *camptodactylia*. This state, which should not be confounded with retraction of the palmar aponeurosis, is observed in arthritics, and consists in the impossibility of fully extending the fingers, particularly the fifth.

EXAMINATION OF THE INTEGUMENTS

A rapid examination of the skin should follow that of the general appearance of the patient.

The *colour* may be modified over the entire body or the greater part of it, or only over a certain region.

In some instances the skin is pale and discoloured. It presents a peculiar white, waxy hue in anæmia; the mucous membranes of the lips, gums, eyes, and genital organs are also pale. At certain points, especially at the lines of the face, a bluish hue is observed, which is particularly pronounced in anæmia of young women and is known as chlorosis. The appearance is so characteristic that the diagnosis is made at a glance. It is well to remember, however, that certain symptomatic anæmias may assume the mask of chlorosis in young women, as is observed, for example, in certain cases of tuberculosis or syphilis, in the course of gastrointestinal disturbances and especially in uncomplicated mitral stenosis.

Chronic intoxications by carbonic oxide, or lead, give rise to somewhat particular anæmic conditions. The same is true of repeated hemorrhages and, above all, metrorrhagias. One of the most typical forms is the anæmia of cancer subjects; their colour is of an absolutely characteristic straw-yellow hue. This appearance, taken in conjunction with the emaciation, permits the observer to confidently diagnosticate the existence of cancer. Of the other affections producing paleness it will suffice to mention pernicious anæmia, leucæmia, amyloid degeneration, and Bright's disease. Acute articular rheumatism deserves special mention because of the intense paleness and profuse odorant sweats characterizing it.

Finally, paleness of the integument may result from vascular spasm; in this case, however, it is transitory. It occurs under the influence of emotion or of anger, during chills, and particularly in leipothymia and syncope.

Congestion of the skin is of quite frequent occurrence, but, as a rule, it is local. In plethoric individuals the red colour is appreciable only on the face and at times in the hands. This condition is known as sanguineous temperament, which appears to be dependent upon a peculiar state of the circulation rather than upon a real augmentation in the amount of blood.

General or at least very extensive cutaneous congestions may occur in the course of a great variety of affections. *Erythema* is then said to exist. In its simplest expression erythema consists in redness which can be dispersed by pressure. In a great many instances, however, a further development of the phenomenon takes place: slight hemor-

rhages or exudations are produced which may simply infiltrate the skin, as in urticaria, or raise the epidermis and thus give rise to bullæ (erythema multiforme).

The redness characterizing eruptive fevers—measles and scarlatina —as well as the rashes occurring as epiphenomenon in the course of most varied infections, particularly at the beginning of smallpox, are nothing more than erythemata.

In order to avoid grave error in interpretation, it must be remembered that in certain individuals, especially in women of nervous temperament, vasomotor disturbances are easily produced. These are generally limited to the face and chest, and become apparent when the physician begins the examination of the patient. They are called pudic erythemata.

Localized redness, especially in the face, may be observed; such, for example, is the redness of the cheeks in pneumonia.

Examination of the integument may also reveal various alterations, some of which are of importance from the standpoint of general pathology, while others, on the other hand, enter into the group of skin diseases. Thus we may find hemorrhages (purpura, ecchymoses), inflammations (erysipelas, eczema), vesicular lesions (herpes) or bullæ (varicella, pemphigus), pustular inflammations (acne, ecthyma, variola), etc. We can not, of course, dwell upon all these lesions, which should always be carefully noted.

Apart from the red colour dependent upon active congestion, there is also a blue colour referable to passive congestion. When the latter hue is general, it indicates profound asphyxia—i. e., a very great disturbance of hematosis. This condition occurs in cardiac or pulmonary insufficiency, and in grave adynamic states, such, for instance, as the algid stage of cholera. In all these cases cyanosis is especially marked in the extremities, hands and feet, the face, and particularly in the lips. It will suffice to remember the appearance of a patient suffering from cardiac disease during the period of asystole.

Cyanosis is local when it is due to compression of a large vessel; it may then serve to diagnosticate an intrathoracic tumour.

The skin may likewise present anomalous colours resulting from the deposition of yellow or brown pigment.

Every one is familiar with the yellow hue of icterus, which first becomes apparent in the conjunctiva, where it must always be looked for, since this localization serves as a point of differential diagnosis from the yellowish hue common to conditions of anæmia, saturnism, malaria, and cancer, which at times recall the colour of icterus.

When there is a deposit of brown pigment, the examination of the mucous membranes is also of great importance. There exists a special

affection connected with alterations of the suprarenal capsules and semilunar ganglia, designated as Addison's disease, and characterized by a brownish colour of the skin and by the presence of brown or slaty spots upon the mucous membrane of the mouth. This latter localization differentiates Addison's disease from other melanodermias, for example, from those observed in consumptives suffering from intestinal lesions, in individuals affected with malarial cachexia, in certain diabetics, etc.

Examination of the integument must include a search for cicatrices. This exploration is sometimes of the first importance, since it may furnish a clew to antecedent pathological occurrences which are unknown to, forgotten, or denied by the patient himself. Of the cutaneous cicatrices some are of traumatic origin and of little importance; others are referable to destructive affections of the skin or mucous membranes, such as acne, ecthyma, variola, tuberculosis, and, above all, syphilis. The syphilitic gummata are frequently seated upon the inner face of the tibia. These consist of round, sometimes confluent and polycyclical lesions; the central portion is colourless, white; the peripheral portion is formed by a brown circle. It is impossible to exaggerate the importance of this stigma which should lead to the institution of specific treatment, the only one capable of saving the patient. It is comprehensible that the smallest cicatrix presents a semeiological value of the highest importance in the case of an individual suffering from aphasia or apoplexy, or fallen into a state of helplessness.

Other cicatrices also possessing a certain importance are represented by vibices. The best known type is that observed in women who have been pregnant: the skin of the abdomen is covered with whitish stripes due to rupture of the elastic fibres. The same lesions occur whenever the skin is too much distended: they are found on the chest during and after a pleurisy; they are also observed in individuals who have rapidly grown; they are of frequent occurrence upon the outer side of the thighs in consequence of an attack of typhoid fever.

After inspection of the skin *palpation* is practised, which furnishes information as to the elasticity, dryness, and temperature of the integument. The skin loses its elasticity to such a degree in grave diseases, especially in affections of the alimentary canal, that it preserves for a moment the folds made on it. This phenomenon is very marked in enteritis of children, in intestinal occlusion, and in cholera.

The skin is thickened and indurated in certain affections, such as ichthyosis, scleroderma, etc. It is dry in grave infections and in diabetics; the return of moisture is a good sign, constituting one of the manifestations of defervescence. In other cases sweats are exagger-

ated, either all over the skin or in certain portions thereof, and they may be of an anomalous character. Coloured, sanguinolent, clammy, and odorant sweats have been recorded. In acute articular rheumatism the body especially is covered with profuse sweats having a strong, almost characteristic odour. The odour of cutaneous perspiration is modified in a great number of morbid states—e. g., in gastro-intestinal dyspepsia, in urinary affections, and in infectious diseases, such as typhoid and typhus fever, cholera, etc.

Palpation likewise furnishes important information in regard to temperature. In some instances it reveals a thermal rise limited to a certain region, and thus leads to the discovery of some local inflammation; in other cases it indicates a general modification. Practice enables one to readily appreciate the variations of cutaneous heat. It should be well known, however, that palpation does not always furnish exact information as to the systemic temperature. There may exist dissociation—viz., the temperature of the skin may at times fall considerably, while central temperature is above the normal. Such, for instance, is the case in the first stage of intermittent fever.

Examination of the skin must be completed by that of its adnexa—i. e., of the nails and hair.

The *nails* often present trophic disturbances. In the course of the most varied diseases they become thin to such a degree that, after the termination, a more or less profound transverse furrow is observed. In other instances they become brittle, and are striated longitudinally. In chronic tuberculosis they thicken, assume the incurvation of a bird's beak over the digital pulp, and, conjointly with the transversal enlargement of the last phalanges, they contribute to impart to the finger that peculiar appearance which is designated as Hippocratic finger.

Analogous trophic disturbances are observed in the hair, which becomes dry, brittle, and easily falls out. Without speaking of affections of the pilous system, we shall confine ourselves to a simple mention of the early baldness of arthritics, and the alopecia of syphilitics, which denudes the scalp in a diffused manner and not infrequently involves the eyebrows.

Examination of the integument may often reveal alterations of the subcutaneous cellular tissue. Œdema, tumours, pseudo-lipomata, and tophi are recognised at a glance, and may guide the physician in his task of clinical analysis. The same is true of dilated veins, the presence of which indicates the development of a collateral circulation and leads to the discovery of deep-seated disorders.

Examination of the Lymphatic Glands.—Either at the beginning of or during an examination the state of the lymphatic glands must be inquired into. In certain instances these glands are so greatly enlarged

as to form tumours readily appreciable at first glance. Tubercular, cancerous, and suppurative glands acquire a considerable volume. In the majority of cases, however, they are to be sought for by means of palpation. Particularly the glands of the neck, groins, and axillæ must be explored, and less frequently the mastoid, the occipital, and the deep-seated glands, while those in the iliac fossa are readily discovered by palpation. The mesenteric, and especially the tracheo-bronchial ganglia, require a more delicate method of exploration, to which reference will be made in connection with examination of the abdomen and thorax.

Ganglionic hypertrophy may be local or general. In the former case it involves a certain group of glands and indicates an inflammatory or other lesion of the corresponding organs. In the latter case, if the subjects are young children and the enlarged glands are numerous but not very voluminous, tuberculosis must be suspected: micropolyadenitis is of great semeiological value. In adults, ganglionic hypertrophy is met with in a great number of acute or chronic infections, notably in syphilis. Finally, more voluminous adenopathies may characterize a particular disease—viz., lymphadenitis.

When an idea as to the state of the patient is formed by means of a rapid general examination, then all the organs and apparatus must be systematically passed in review. It makes no difference with what part of the body examination begins; the observer will generally be guided by the first information acquired. The disturbances first experienced, the seat of pain, and the results of interrogation serve as guides. It is therefore well to begin with that apparatus which appears to be most affected. With a patient who complains of pain in the side, coughs, and breathes with difficulty, the chest is first examined; with another suffering from intestinal disorders, attention is first given to the abdomen; in still other instances, the nervous system is first reviewed. Even when a diagnosis appears to have been perfectly determined by the examination of one apparatus the rest of the organism must always be systematically explored. This is the only way to avoid gross errors.

We shall therefore review the principal rules presiding over clinical examination. We shall indicate the usual procedures which can be utilized by the physician without the aid of any instrument. This method of exploration, which is, as a rule, sufficient to lead to diagnosis, may, however, be completed by more delicate procedures; but the latter, requiring special knowledge and highly complicated instruments, do not admit of current use in daily practice. They will be briefly referred to in the next chapter.

Examination of the Circulatory Apparatus

The physician may have already been guided to a diagnosis by the information furnished by the patient. Paroxysms of dyspnœa, particularly of that dyspnœa designated as dyspnœa of effort; presence of a slight perimalleolar œdema in the evening; palpitation, præcordial pain, and a phenomenon of far greater importance—i. e., attacks of angina pectoris—are the disturbances which draw the physician's attention to the heart. The facies of the patient also guides the investigation. The special mode of lying, the bluish hue, and the throbbing of the jugular veins in a mitral patient have already been referred to.

Examination of the circulatory apparatus must be conducted with a strict method. It is well to begin, not with the heart, but with the pulse. By means of palpation of the radial and the temporal arteries it must first be determined whether arteriosclerosis exists. The beatings which may involve certain arteries, especially their flexuous ramifications, must be carefully noted. They can be made out by means of inspection of the vessels of the elbow joint, temple, and neck. Abrupt movements of extension produced at each cardiac systole are observed in arteriosclerotics and aortics, and are known as the dance of arteries.

After this first inspection the pulse is felt and its frequency registered. Its strength and fulness is determined, and whether it is regular and equal. The pulse is irregular when its pulsations are not separated by equal intervals; it is said to be unequal when the successive beats do not possess the same intensity or volume. It must also be noted whether the pulse is full or compressible. In the former case the artery remains sufficiently open after beating; in the latter, it empties itself abruptly. A strong but compressible pulse immediately suggests an aortic insufficiency (Corrigan's pulse). It is possible to exaggerate these characters by raising the patient's arm; it is readily understood that the depression consecutive to the cardiac systole is thus made more apparent. In such cases the examination must be completed by a research of " capillary pulsation," a name designating the alternation of redness and paleness visible in richly vascular parts of the body, such as the forehead—after friction is made in order to increase the influx of blood—the nails, and the palate. It is well, moreover, to feel the various arteries, especially those of the neck, in order to note the presence or absence of thrill, which is particularly frequent in cases of aortic insufficiency.

Without dwelling on other peculiarities which may be presented by the pulse, we must mention dicrotism. This is the exaggeration of a

normal phenomenon—viz., the arterial pulsation is followed by a second slighter shock.

Examination of the Heart.—After these first inquiries as to the state of the circulatory apparatus, examination of the heart is taken up.

Inspection.—It is necessary for the patient to be in the reclining posture at the time of this examination. This rule admits of no exception. He must lie upon his back, and the physician should place himself at his left side, and then take such a position as to bring his face down to the level of the patient's thoracic wall. Examining the præcordial region in this position, he will clearly see, unless the subject be obese, under normal conditions, the apex beat, about 2 centimetres below the nipple. Under pathological conditions the impulse may be stronger or weaker, and it may even be imperceptible. The apex beat may be displaced downward and outward. The præcordial region may present a general vaulting or a limited pre-eminence, which may at times be very pronounced and even pulsating, as occurs in case of aneurism. In certain instances a more delicate phenomenon is observed—viz., the systolic retreat of the apex—indicating a pericardiac adhesion, and often attended by an undulating movement of the præcordial region.

Palpation.—A second mode of examination is represented by palpation. The intensity and extent of the cardiac impulse and the existence of thrilling can be made out by the hand flatly applied to the præcordial region. Then an exploration is made with one finger with a view of determining exactly the point at which the impulse takes place, as well as the point of the thrill, should any exist, and, finally, the sensitiveness of the organ. Peter has justly laid stress upon the importance of the pain which is produced by pressing upon the heart in cases of myocarditis or pericarditis. Palpation is mostly resorted to for determining the position of the apex beat. One finger is fixed at the point where the pulsation is felt, then with the other hand the intercostal spaces are counted. In this manner it is learned that, under normal conditions and in the reclining position, the apex beat is situated at the fourth intercostal space. It is often said simply that it beats below the nipple. This point of comparison is very simple and convenient, but it is not precise, especially in women, whose mammary glands are often distended or hanging; variations are therefore too considerable to permit the use of this point of localization.

Even in the normal state the situation of the apex beat varies with the position assumed by the patient. When he lies upon the left side, the beat is displaced 2 to 5 centimetres; when he lies upon the right side, the point of pulsation is not changed. In the standing

position it is somewhat lowered and deviates outward. It is likewise important to know that in children the apex beat is located 2 or 3 centimetres outside of the nipple under normal conditions.

After having determined the place where the shock is produced, its intensity should also be noted. In order to accomplish this, the examiner must be familiar with the practice of palpation and have preserved the memory of the tactile sensation obtained in normal individuals of the same age and nearly the same degree of muscular and adipose development as the subject under examination.

Palpation next informs us as to the cardiac rhythm—that is, as to the regularity and equality of the beats. When the beating is irregular, it is well to examine simultaneously the heart and the radial artery. In fact, a curious discordance between the rhythm of the heart and that of the pulse is observed in some cases. False intermittences are said to exist when no cardiac irregularity corresponds to the radial irregularity; in this instance there is simply cardiac inequality; the weakest beats are not transmitted to the periphery.

If palpation is practised with sufficient care, information of the first importance is at times acquired for diagnosis. Indeed, it is possible to thus perceive murmurs which are too often looked for by means of auscultation alone. When the murmur is vibrating, it is expressed by a purring tremor readily appreciable by palpation; if the pulse be examined at the same time, it can easily be learned at what instant of the cardiac revolution this tremor is produced. It is even easier to determine its seat, and palpation renders good service in this regard as well, since the murmurs are propagated and auscultation always permits location of them as precisely as does palpation. Mitral stenosis especially may be diagnosticated without the aid of auscultation. By means of this same procedure certain other phenomena may also be perceived—for instance, pericardiac frictions and often galloping murmur.

Percussion.—After palpation, percussion is practised, proceeding from the sonorous toward the nonsonorous parts. Two zones are thus delimited: a peripheral zone, which is dull, and corresponds to that portion of the heart which is covered by the lung; and an internal zone, triangular in shape and of absolute flatness. The first begins from the left border of the sternum, at the lower part of the second rib, and is limited by a curved line reaching the apex. The zone of flatness begins lower down at the level of the fourth rib, and terminates also at the apex. The flatness of the lower part of the heart is confounded with the flatness of the liver. In order to outline the right border of the heart, we must percuss below the right nipple;

when the upper limit of the liver is obtained, it must be united to the apex by a straight line. Then we must delimit, on the right side of the sternum, the dull zone which is produced by the prominence of the organ. Finally the aorta is percussed, which normally gives a dulness of 2 centimetres on the right side of the sternum.

Cardiac flatness varies considerably under various pathological conditions. Without describing the phenomena that may be observed, we shall give simply a summary of the principal modifications.

1. Hypertrophy of the left ventricle: The apex is displaced downward and thrown outward. The line marking the upper limit of flatness is raised and passes above the nipple.

2. Hypertrophy of the right ventricle: The apex beat is pushed slightly outward; the line limiting the flatness passes a little above the nipple, and there is a notable zone of flatness on the right side of the sternum.

3. Pericardial effusion.

a. If the fluid is not very abundant, it accumulates in the infero-external angle of the pericardium; flatness is found at a point below the apex beat.

b. When the effusion amounts to about 400 grammes, the flatness takes a peculiar form, known as flatness in the shape of a coffee-ring cake (en brioche); at the upper part a quite characteristic notch is found (Sibson's notch).

c. In cases of profuse effusions, flatness is triangular in shape, with the base down. The right side of the triangle is less oblique than the left.

Auscultation.—The last and the most important mode of exploration is auscultation. As the physician must place himself at the left side of the patient, he will consequently auscultate with his right ear. It is better, however, to acquire the habit of auscultation with either ear. Moreover, it is well to feel the pulse of the subject while listening to the pulsation of the heart, in order to readily determine the time of the cardiac revolution.

Although it is not an absolute rule, it is preferable to begin auscultation with the base and explore successively the aortic orifice in the right second intercostal space, then the pulmonary orifice in the left third intercostal space, the mitral orifice at the apex beat, and finally the tricuspid orifice at the xiphoid appendix.

Two sounds are heard under normal conditions. The first or the systolic corresponds to contraction of the ventricles; it is customary to represent it by a brief (⌣). Then comes the brief silence, and after this the second or diastolic sound, which coincides with the closure of the semilunar valves; this is represented by a long (—).

Finally, another period of silence is produced, that is the long silence, after which the movements are repeated.

The object of listening to a heart is to determine the force of the impulse; the relationship between cardiac and arterial pulsations; the modifications of rhythm and pitch, and whether any pathological murmurs are superadded to or replacing a normal sound.

In order to appreciate the force of pulsations, one must have listened to a great number of healthy hearts. The ear preserves, as it were, the memory of the physiological sounds and perceives very exactly the changes which occur. It should be borne in mind that these modifications may vary from one orifice to another. Hence, an exaggeration of the second sound is quite frequently met with at the pulmonary orifice, indicating nothing more than some disturbance in the circulation of the lung.

Diminution in the intensity of the cardiac sounds may be due to several causes. In some instances it depends simply upon the exaggerated obesity of the subject; in others it is referable to weakness of the myocardium, and then it is the first sound that grows dull and finally disappears. This phenomenon, while very serious, is, however, of less gravity than weakness of the second sound. Lastly, the heart beats may grow weak and even become imperceptible as the result of effusion within the pericardium. In the latter case, when the fluid is not too abundant, it is possible to perceive the sounds through a stethoscope pressed well upon the chest when the patient is in the sitting posture with the body inclined a little forward.

The disturbances of the cardiac rhythm may be divided into two groups: *intermittence* and *arrhythmia*.

In case of intermittence the series of pulsations is from time to time interrupted by a more or less periodical suspension. The patient is not infrequently conscious of these arrests, and justly notices that suppression of a beat is followed by a systole of far greater energy.

Arrhythmia is divided into regular and irregular. The irregular comprise: (1) The false steps—i. e., irregularities in the succession of heart beats. (2) Chronological perversions characterized by a too prolonged duration of some one of the heart beats or of one of the periods of silence. Regular arrhythmia includes (*a*) the cardiac *bigeminia* and *trigeminia*—viz., the production of two or three beats one after another, followed by a sufficiently long pause; (*b*) the *alternating pulse* (Traube), characterized by one strong beat followed by a weak pulsation, whether bigeminia be present or not; (*c*) the *coupled rhythm* of the heart, when the cardiac revolutions are coupled, so to say, in strokes of two; the first of the couple is strong, the second is so weak that it is not perceptible at the radial artery except when a

registering apparatus is employed; (d) lastly, under the name of alternating pulse, cases have been recorded by Dr. Bard in which a series of strong pulsations is followed by one of weak strokes.

The cardiac rhythm may also be modified by certain changes occurring in the relations or intensity of each heart beat. For example, the two sounds may become equal, then the duration of the two periods of silence, and the pitch as well as the intensity of the two beats become similar. In this event, the frequency being augmented at the same time, the ear perceives exactly the same rhythm as when a fœtus is auscultated. Hence the name *fœtal rhythm* justly given by Stokes to cases of this kind. This phenomenon, which is observed in acute myocarditis, possesses great semeiological importance and is of highly unfavourable prognostic significance.

The rhythm may be modified as a result of the *decomposition* of one of the sounds. In most cases it is the second sound that is decomposed. The result is a rhythm with a triple sound made up of one brief and two long sounds following each other very closely. This is the *murmur of recall (bruit de rappel)*, which may be encountered in normal subjects; in this case, however, it is intermittent and transitory, and is due to the fact that the two sets of semilunar valves do not close simultaneously. This is what occurs in pathology when some disturbance of the pulmonary circulation modifies the play of the valves—e. g., in mitral stenosis.

In some rare instances—not so rare, however, as most authorities believe—the rhythm with three sounds is due to the breaking up of the first sound. The author has frequently met with this rhythm in auscultating at the base of the xiphoid, but it has been impossible to determine its pathological significance.

Auscultation frequently reveals an additional sound preceding the systole; this is the *galloping murmur*. The superadded sound constitutes a tactile rather than an auditory phenomenon; it depends upon an abrupt distention of the ventricle, whose elastic force has increased at the expense of the contractile power. It is therefore readily perceived by palpation, and it is thus possible to recognise that it precedes the first sound and is independent of it.

The galloping murmur is perceived in two different places. In most cases it is a galloping murmur of the left heart, and is heard a little inside of and above the apex beat, resulting from alteration of the myocardium. It is of very frequent occurrence in sclerosis of the heart, and generally accompanies interstitial nephritis. A second variety, far less frequent, is the galloping murmur of the right heart, which is heard over the xiphoid appendix and indicates gastrointestinal, oftener hepatic, disorders, particularly colic of lithiasis.

The modifications above referred to may easily be represented in a schematic manner:

a)   ∪ —   ∪ —   ∪ —   ∪ —   ∪ —

b)   ∪ —   ∪ —   ∪ —   ∪ —   ∪ —

c)   ∪ _ _   ∪ _ _   ∪ _ _   ∪ _ _   ∪ _ _

d)   ∿ —   ∿ —   ∿ —   ∿ —   ∿ —

e)   ◡∪ —   ◡∪ —   ◡∪ —   ◡∪ —   ◡∪ —

f)   ◡

Legend

Normal rhythm...................	a	Decomposition of the first sound....	d
Bigeminated rhythm.............	b	Galloping murmur................	e
Murmur of recall................	c	Fœtal rhythm...................	f

The rhythm may also be modified by additional murmurs originating in the pericardium. These are *frictions*, the name of which is sufficient to indicate the character. They have been compared to the murmur produced when paper is crumpled or to the creaking of new leather. They may accompany the two movements of the heart or one of the two periods of silence. The murmur is, as a rule, one of a to-and-fro character. When the friction occupies one of the periods of silence it produces a rhythm with three sounds, which must not be confounded with the galloping murmur.

The *blowing murmur* is comparable to that produced when bellows are blown in making a fire (Laennec). The murmur is said to be *systolic* when it covers the first movement of the heart; *diastolic,* when it accompanies the second; *mesosystolic,* when it occurs during the brief silence; *presystolic,* when it precedes the first sound; it then coincides with the contraction of the auricle, and therefore should be called *auricular systolic.* In case one has not yet become well accustomed to auscultation, it is better to feel the pulse while listening to the heart; the murmurs accompanying the radial pulsation are systolic; those which precede it are presystolic; those that follow it are mesosystolic. The diastolic murmurs are readily recognised, since they accompany the second sound, and are, as a rule, gentle and aspiratory.

The following table shows the relationship existing between the various movements of the cardiac revolution and the murmurs that are met with:

FIRST MOVEMENT.	SHORT SILENCE.	SECOND MOVEMENT.	LONG SILENCE.
Ventricular systole. Shock of the apex. Radial pulse. Systolic blowing murmur.	Mesosystolic blowing murmur.	Closure of the semilunar valves.	Diastole, auricular systole. Presystolic murmur.

The first thing to do is to time and locate the murmur. In doing this the stethoscope is often of valuable service. When this is done, it is, at least theoretically, quite easy to draw conclusions. It will suffice to remember the physiological state of the heart at the moment the murmur is produced.

During the systole the ventricles contract; if the seat of the murmur is at one of the auriculo-ventricular orifices, it is because the blood flows backward from the ventricle to the auricle; there is then insufficient closure, or, as is said, *insufficiency* or *incompetency* of one of the auriculo-ventricular valves. When the murmur is heard at one of the arterial orifices, it indicates that this orifice does not allow the blood to pass through it as easily as under normal conditions, this being due to diminution of its calibre. *Stenosis* is then said to exist.

When the murmur is diastolic and coincides with the second sound, it means that the blood flows backward from the arteries into the ventricles; there is aortic insufficiency, and, exceptionally, insufficiency in the pulmonary artery. The diastolic murmur heard at the apex has particular characters; it is a rolling rather than a blowing sound. It is produced by stricture of an auriculo-ventricular orifice, nearly always of the mitral. The significance of the presystolic murmur is the same.

These varieties of murmurs may very readily be understood by examining the following table:

MURMURS.

Systolic ....
- At the base .
  - To the right of the sternum. — Aortic stenosis.
  - To the left of the sternum. — Stenosis of the pulmonary artery (quite rare).
- At the apex................. — Mitral insufficiency.
- At the xiphoid appendix...... — Tricuspid insufficiency.

Diastolic ...
- At the base .
  - To the right of the sternum. — Aortic insufficiency.
  - To the left of the sternum. — Pulmonary insufficiency (exceptional).
- At the apex................. — Mitral stenosis.
- At the xiphoid appendix...... — Tricuspid stenosis (rare).

Presystolic..
- At the apex................. — Mitral stenosis.
- At the xiphoid appendix...... — Tricuspid stenosis (rare).

Without dwelling on the characters of murmurs, we shall only recall that the murmur of mitral insufficiency is often a whistling, sometimes a musical or piping one. That of aortic insufficiency is mild, soft, and blowing. That of mitral stenosis is rather analogous to rolling. Finally, a systolic, forcible, vibrating murmur is at times heard in the centre of the præcordial region, unattended by purring tremor; it means inocclusion of the intraventricular septum. In this case, and when there is stenosis of the pulmonary orifice, it is well to auscultate the back of the patient. Over the fourth dorsal vertebra a murmur is heard indicating the persistence of the arterial channel; it is due to a lesion of compensation occurring quite frequently in cases of congenital malformations of the heart.

When a murmur is found, timed, and located, its propagation must then be determined. This is of considerable importance in definitely locating the murmurs, and especially for distinguishing those due to cardiac lesions from those produced independently of any alteration of the heart and which constitute nonorganic murmurs. This distinction is not always easily made; it presents great interest, however, for the reason that organic murmurs are signs of grave lesions, while nonorganic have no prognostic value.

Nonorganic murmurs are usually mesosystolic, exceptionally diastolic or rather mesodiastolic. They are soft, blowing, and superficial; they easily vary from one moment to another; they are best heard at the end of inspiration, and disappear at the end of expiration. Taking ground on this last character, Professor Potain ascribes to these murmurs a pulmonary origin. They are due to the fact that the systolic contraction imparts to the anterior border of the lung movements which cause the expulsion or the aspiration of a certain amount of air. According to this pathogenesis, it is comprehensible that these murmurs should be heard exclusively in those parts of the heart which are in contact with the lungs. In the mitral area the organic and the nonorganic murmurs occupy the apex. But whenever a murmur is heard either outward or inward from the apex or at the left border of the heart, it can be pronounced as nonorganic. Of course organic murmurs may be conducted into these regions, but the nonorganic or extracardiac murmurs alone are localized therein. In the aortic area murmurs are nearly always organic. In the pulmonary area they are sometimes organic and at other times nonorganic. The same is true along the left border of the sternum and at the ensiform cartilage, although in these last two areas nonorganic murmurs very seldom occur.

Extracardiac murmurs are attenuated when the subject takes the standing posture; then, in fact, the heart comes more directly in con-

tact with the thoracic wall. For the same reason they likewise disappear during an effort. If the patient can frequently be auscultated, daily modifications are observed, and even disappearances. It must also be borne in mind that nonorganic murmurs are incapable of propagation. This fact is of great consequence, since organic murmurs present propagations which are very important to know. Mitral murmurs, for example, are conducted into the left axilla and are heard behind, especially in children, under the angle of the scapula. It is therefore necessary that these areas should always be included in the auscultatory examination.

The murmurs of the pulmonary orifice are conducted toward the left clavicle; they suddenly stop before reaching this bone. Aortic murmurs are extended toward the right clavicle, which they reach and often go beyond, since they are still audible in the vessels of the neck. In a great number of instances the diastolic murmurs of the aortic orifice follow another direction. They are propagated along the sternum, from above downward, and are very clearly heard at the xiphoid appendix; in certain cases their maximum occupies the apex, in others the left portion of the sternum. Notwithstanding the variability of localization, interpretation is easy. The murmur of aortic incompetency presents special characteristics and is attended by phenomena which do not permit of error. As already stated, it is a soft, blowing murmur, so peculiar that no other lesion can simulate it except at times some extracardiac murmur or friction. There are, however, manifestations accompanying the murmur which settle the diagnosis: these are a jerking pulse, called Corrigan's pulse, throbbing or dance of the arteries, the intermittent double crural murmur, and capillary pulsation.

In the way of practical conclusion it may be said that auscultation at the classic foci is not sufficient; the propagations of murmurs must also be looked for. In order to obtain positive information as to the nature and site of murmurs, the ear should be applied to spots far removed from the areas where they are produced. Extracardiac murmurs are produced and expire on the spot, while intracardiac murmurs are diffuse. Before they can be declared to be organic, apex murmurs must be heard in the axilla, and even in the back; and basic murmurs must be conducted through the vessels emanating from the affected orifice or along the sternum.

In case a murmur should be diffuse and is heard at two orifices, it is often difficult to tell whether we have to deal with a single murmur or two different ones. Judgment should be based especially on the pitch. When a murmur is heard in one area and is propagated to another orifice, still preserving the same acoustic characters, al-

though weakened, it is possible to affirm with certainty that the lesion is single.

When two differently timed murmurs are heard, it should not be hastily concluded that two lesions exist. For instance, a double aortic murmur—namely, a systolic followed by a diastolic murmur, does not necessarily mean a double aortic lesion—i. e., a stenosis with insufficiency. In a great number of instances aortic incompetency is attended by a systolic murmur which simply depends upon the roughened condition of the orifice. Finally, when a diastolic blowing murmur is heard along with a presystolic murmur of the apex, it does not necessarily follow that there is aortic insufficiency with mitral stenosis. A simple aortic incompetency may give rise to both murmurs. According to Flint, the presystolic murmur is due to the vibration of the mitral valves caused by the blood current. According to Keyt, it is produced at the beginning of systole.

Examination of the Peripheral Vessels.—Examination of the circulatory apparatus is terminated by the study of the peripheral vessels. As already stated, the pulse must first of all be felt and flexuosities of the arteries looked for. After exploration of the heart the condition of the vessels may again be studied, if there is reason for so doing. If aortic dilatation is suspected, palpation should be practised above the clavicles in order to determine whether the subclavian arteries, particularly that of the right side, are not raised. The fingers should be pressed above the manubrium to discover whether the dilated aorta is not bulging there. The neck of the patient must next be examined to decide whether any arterial pulsations, and especially venous pulsations, exist. In the case of tricuspid insufficiency, the blood regurgitates into the auricle and vena cava during ventricular systole. It thus imparts a series of pulsations to the brachiocephalic venous trunks; when the valves supplying these veins yield, the blood easily flows back into the jugulars. The latter then pulsate like arteries; this is *venous pulse.* By pressing the blood from below upward, it is easy to see that the lower portion again becomes full; this minor exploration thus enables the physician to conclude as to the unquestionable presence of venous regurgitation.

Palpation may also reveal the existence of arterial thrill. In cases of aortic incompetency a thrill is found particularly in the carotids, at times so intense as to first suggest aneurism.

Furthermore, auscultation of the arteries should not be overlooked. Arterial and venous sounds are to be sought for in the neck. Arterial murmurs may be due to propagation of some aortic murmur or to the presence of an aneurism of the carotid or aorta. Venous

murmurs are commonly nonorganic. The most important is that of chlorosis; it is a continuous murmur (*bruit de diable*) with systolic re-enforcement.

When aortic incompetency is suspected, the stethoscope must also be applied to the femoral artery at the base of Scarpa's triangle. The ear there perceives a double murmur, which has been well studied by Durozier.

In brief, the diagnosis of a heart lesion can only be made in a precise manner by taking into consideration a whole series of phenomena. Examination of the heart is not sufficient. This must be supplemented by examination of the vessels for the diagnosis and by that of various organs for the prognosis. We are thus led to speak of the other viscera. The respiratory apparatus will first be considered.

EXAMINATION OF THE RESPIRATORY APPARATUS

LARYNX.—Examination of the larynx can hardly be made without special instruments. It is possible, however, to acquire some information concerning the state of this organ by questioning the patient, and especially by interpreting certain functional derangements.

The patient complains of pains during deglutition; he often succeeds in locating them precisely: the trouble is not in the throat, but farther below, in the neck, and pressure upon the larynx gives rise to painful sensations, which serve to establish the diagnosis. Phonation is sometimes painful, and always disturbed; the voice does not possess its normal quality; it is hoarse, bitonal, or multitonal. At a more advanced stage the patient is unable to speak except in a whisper.

The phenomena become complicated when the passage of air is hindered by various causes, such as partial destruction with secondary vegetating productions, cicatricial stricture, swelling of the mucous membrane or subjacent parts, as occurs in the œdema of the glottis, formation of pseudo-membranes in croup, and in the presence of a foreign body or a polypus. Under these conditions the obstruction of the air passage is expressed by a special facies and a series of manifestations of semeiological importance. Dyspnœa is experienced during inspiration; the air penetrates but slowly, often giving rise to a hissing murmur, and, particularly in young subjects, to a depression above the sternum, known as suprasternal retraction. At the same time, especially if the obstacle is very troublesome, each contraction of the diaphragm is attended by the formation of a furrow along the border of the false ribs; this is called infrasternal retraction. These phenomena, which are very striking in diphtheritic laryngitis,

indicate the necessity of operative intervention—tracheotomy or intubation.

A relatively simple examination thus makes evident that the dyspnœa depends upon laryngeal alteration. In a great many instances the signs just described are the only ones to be considered. Laryngoscopic examination is useless and even dangerous in a patient suffering from asphyxia. Auscultation of the larynx, which reveals the so-called flag murmur in case of pseudo-membranes, is a procedure seldom resorted to.

BRONCHI AND LUNGS.—When the other parts of the respiratory apparatus are in question, attention is directed to their alterations by the various symptoms described by the patient. These are pain in the side, dyspnœa, cough, and expectoration.

Subjective Symptoms.—The pain in the side is commonly referable to irritation of the intercostal nerve, produced by inflammation of the pleura. To enumerate the causes capable of giving rise to this inflammation would be to cite all the affections which attack the pleura primarily or secondarily. The principal conditions are pleurisy, pneumothorax, inflammation of the peripheral parts of the lungs, whatever their nature, pneumonia, broncho-pneumonia, gangrene, embolism, or tuberculosis. The pain is spontaneous, and is aggravated by movement and cough; it is often exasperated by palpation. In certain instances it irradiates toward the hypochondrium and loins. When there is diaphragmatic pleurisy, pain is produced by pressure with the finger either over the course of the phrenic nerve, between the scalens, or along the left border of the sternum, or else at a point situated at the intersection of the prolongation of the sternal border and the tenth rib. This is the diaphragmatic button of Guéneau de Mussy.

Dyspnœa is equally a subjective and an objective phenomenon. The patient complains of oppression, and the physician notes certain changes in the respiratory rhythm, to which reference will be made in treating of inspection.

Cough is an abrupt contraction of the expiratory muscles attended by spasm of the constrictors of the glottis. It is a reflex phenomenon whose point of origin may be found in the most varied parts of the organism—e. g., the external auditory canal, the tonsils, the alimentary canal, the liver, and the spleen. In thoracic affections it presents certain peculiar characters connected with its origin or the lesion exciting it. At times it is dry, as is observed in pleurisy and in the beginning of most pulmonary affections. It becomes moist as soon as bronchial hypersecretion is produced, and it is then accompanied by expectoration. Cough may occur in isolated efforts in " spells." In bronchial dilatation the patient on awakening rejects by long paroxysms of cough

purulent liquids accumulated during the night. In the beginning of tuberculosis cough appears in the morning, toward 5 A. M. In whooping cough the paroxysmal character is most manifest. There then occur several series of coughing separated by a hissing inspiration, all ending in the expulsion of a viscous fluid. The name " whooplike" (*coqueluchoid*) has been given to a cough similar to whooping cough, but less hissing, and commonly connected with a hypertrophied condition of the tracheo-bronchial glands.

Furthermore, according to its acoustic characters, cough may be sonorous, hoarse, or hissing.

Although cough possesses no more than a restricted value from a semeiological standpoint, it acquires considerable importance by the products which it expels to the exterior. Expectorations must be carefully studied. We shall first consider the results furnished by a simple examination with the unaided eye; in most cases this is the only mode of exploration which can be resorted to, and we shall see that it generally affords the physician sufficient information.

Expectorations.—Sputa may be serous, mucoid, seropurulent or mucopurulent, or sanguinolent.

Serous sputa, consisting of a frothy, aerated fluid, are quite rare; they are met with in asthmatiform bronchitis of arthritics and in cases of so-called albuminous expectoration, which is sometimes observed in consequence of thoracentesis.

Expectoration is tenacious and colourless in acute pulmonary congestion and splenopneumonia.

Mucoid sputa, consisting of a transparent, glairy, colourless, aerated, and frothy fluid, expresses simply a bronchial hypersecretion; they are observed in bronchitis, at least in the beginning. In tubercular cases they sometimes contain small purulent particles, and, after a paroxysm of asthma, small dry, elastic, and granular masses.

In plain (lobar) pneumonia the sputa are mucoid, but possess an absolutely characteristic appearance: they are viscous, thick, adhering to the vessel, and rusty in colour. Their semeiological importance is very great for the reason that in central pneumonia, auscultation revealing no disorder, they constitute the only certain sign of the disease.

Mucopurulent expectoration is of very frequent occurrence. It is observed in the second stage of acute bronchitis, in chronic bronchitis, and in tuberculosis. In the last-named disease the sputa have a special appearance, on account of which they have been called *nummular sputa.* They are large round or oval flat masses swimming in a mucoid fluid and remaining clearly separated when placed in water. This very important expectoration is not, however, absolutely pathog-

nomonic; it is also found in bronchial dilatation, influenza, and measles.

Mucopurulent expectoration may be coloured by the substances inhaled by the patient. Hence it is black in anthracosis and red in siderosis.

Purulent sputa form at the bottom of receptacles a greenish-yellow mass having the appearance and odour of pus. They are encountered in the last stages of acute bronchitis, influenza, caseous pneumonia, and particularly in dilatation of the bronchi. In the morning the patient empties his bronchial cavities which were filled during the night.

In certain instances a patient is seen to suddenly expel a considerable amount of pus through the respiratory passages. This is designated as *vomique*. Three causes may give rise to it. It sometimes results from a pulmonary abscess opening into the bronchi, in which case the pus is usually thin and reddish; at other times it is due to the opening of a purulent pleurisy, at times occupying the great pleural cavity, but in most cases being confined to a limited spot. These are generally cases of metapneumonic and especially interlobular pleurisy; the pus is quite copious, somewhat thick and greenish. Finally, a third variety, more difficult of diagnosis, is represented by those cases in which an abscess, formed in a neighbouring region, opens into the bronchi; suppurations of the liver, kidneys, and mediastinum, and abscess caused by congestion, are the most frequent agencies.

Expectorations may also contain more or less organized productions, such as pseudo-membranes proceeding from the larynx, at times from the trachea or bronchi, in some cases presenting a ramified appearance, reproducing the ramifications of the respiratory passages. These productions are seldom met with in diphtheria, but more frequently in a type of chronic bronchitis which for this reason is designated as pseudo-membranous.

There may also be found membranes or detritus of hydatids, or minute granules of a yellow colour, indicating an actinomycotic focus opening into the lungs.

Finally, expectoration may contain variable quantities of blood, under which circumstances it is called *hemoptysis*. Of this two principal varieties are admitted. At times the blood is red, aerated, and frothy, as is the case in hemoptysis of bronchial origin; it is of frequent occurrence, and is the type encountered in tubercular subjects. At other times the blood comes from a pulmonary hemorrhage; an infarction, or, in other words, a pulmonary apoplexy, has taken place. These sputa, described since the time of Laennec as hemoptoic, are, unlike the preceding variety, dark, thick, viscous, and nonaerated; they adhere to the walls of the vessel containing them and exhale an

acrid odour. This kind of expectoration is observed in cardiac patients, particularly in mitral stenosis, in the course of infectious or chronic dyscrasias, such as Bright's disease, and as a result of embolism.

Bronchial hemoptysis may be sufficiently profuse to cause death; it is not, however, prolonged after the occlusion of the vessel from which it issued. Pulmonary hemoptysis is less abundant, but it lasts several days in succession, since the lungs require a certain length of time to rid themselves of the blood infiltrating the parenchyma.

Not unlike these two varieties is the expectoration having the appearance of currant jelly; it is met with in cases of pulmonary cancer.

A last advice is to smell expectorations. Their odour possesses great semeiological importance, especially in cases of fetid bronchitis and pulmonary gangrene. The odour often leads to the diagnosis of a sphacelated focus.

Examination of sputa may be completed by microscopical and bacteriological researches, the principles of which will be referred to in connection with diagnosis.

Physical Signs.—Inquiry into the physical signs is conducted in the same manner as in the case of the circulatory apparatus. The general appearance of the patient is first noted. The exact number of respiratory movements per minute is registered, and it is often of interest to determine the relationship existing between the frequency of respiration and that of the pulse. Under normal conditions the respiration rate is 16 and that of pulse 80 per minute; that is, a ratio of 1.5. It is equally easy to make out the amplitude, form, and rhythm of respiration. The movements may be more or less profound than in health, they may also be unequal or irregular.

In certain instances respiration presents peculiar rhythm, of which there are three notable types:

Cheyne-Stokes respiration is especially observed in cerebral or meningeal lesions, particularly in tubercular meningitis, as well as in certain auto-intoxications, such as uræmia. It is characterized by the following rhythm: The respiratory movements are at first rapid and superficial, then they become more and more profound; this is followed by a gradual diminution in the amplitude of the movements, which are finally arrested; there is apnœa for a few seconds and then breathing is again resumed, at first hardly perceptible, but becoming progressively fuller. These various phenomena thus follow each other in regular alternation.

Kussmaul's respiration occurs in diabetic coma. It is characterized by an abrupt and deep inspiration, followed by a pause, then by a quick expiration and a new pause.

These two respiratory types are probably referable to disturbances of the medulla; at all events, they are independent of pulmonary lesions. With the *expiratory breathing of Bouchut* we return to our subject. This peculiar type of respiration is met with in children suffering from broncho-pneumonia. It is, as it were, the reverse of the normal type. Breathing begins with a brisk expiration, followed immediately by an inspiration; repose takes place after inspiration instead of after expiration.

As already stated, the mode of breathing and the important deformities of the chest are noted by means of inspection. Previous diseases may have produced deformities which disturb the regular play of the lungs and thus favour alterations of this organ. Pott's disease and rickets often cause extensive deviations in the form of the thorax. In other instances the defective conformation results from occupations which necessitate certain movements or certain attitudes. These facts are not without importance, but they act only as predisposing causes.

Deformities connected with alterations of the respiratory apparatus may be general or partial.

General deformities occur under two principal forms.

In emphysema the lungs, having become too voluminous, give rise to dilatation of the thorax. The chest is rounded and, in advanced cases, is deservedly called "barrel-shaped." The sternum is pushed forward, the intercostal spaces are no longer visible, the supraclavicular depressions disappear, the neck is shortened, and the head appears to be borne directly upon the shoulders.

The consumptive's appearance is just the reverse of the preceding. The chest seems to be elongated, the eminences are more apparent than in health, the interspaces are more conspicuous, the scapulæ are protruding, and the muscles atrophied. If a slight percussion is practised, fibrillary contractions (*myoidema*) appear beneath the skin covering the muscles, especially the pectoral muscles.

The partial deformities of the chest consist in bulgings and retractions.

In tumours of the mediastinum and in pleural effusions, one half of the thorax is increased in size; it sometimes assumes a rounded shape and imparts to the chest the appearance described as oblique oval. In order to well appreciate these deformities the following procedure may be resorted to: One end of a string is held by a finger at the upper part of the sternum at equal distance from both clavicles; the lower end is then brought to the pubis. Under normal conditions the string divides the anterior part of the thorax into two equal halves; it therefore traverses the middle of the sternum. In case of effusion

or tumour, the point of the sternum is deviated toward the diseased side, and the deviation to one side of the middle line measures the degree of deformity.

Instead of bearing on one side of the chest, as in the example above described, the deformity may be local and express a more extended tumefaction. Such is notably the case with purulent pleurisies. The impulse of the heart is sometimes transmitted to this tumefaction, thus constituting the pulsatile empyema which may be mistaken for an aneurism.

Certain functional derangements disturb the expansion of the thorax. As a result of intense pain or of some inflammatory lesion in the neighbourhood of the diaphragm, the breathing becomes far less deep upon one side than upon the other; it may even be arrested on the affected side, resulting in manifest asymmetry during inspiration.

Partial deformities may consist in retractions. In cases of chronic pleurisy the persisting adhesions give rise to retraction of the diseased side. Laennec has laid great stress on this type of alterations, of which he has given a figure that has become classical.

These various alterations of the thorax sometimes produce skin lesions. When there is exaggerated expansion the skin cracks and presents vibices, which persist for an indefinite period and at times serve for retrospective diagnosis.

Finally, examination of the integument may reveal œdema of the thoracic wall, an important phenomenon, for, in case of pleurisy, it is a sign pointing to the purulent character of the collection. Less frequently a subcutaneous emphysema is found due to the presence of gas bullæ proceeding from some minor fissure in the respiratory apparatus.

The results afforded by inspection should be completed by *mensuration*. It is possible to obtain important information by means of bimanual palpation. The patient being in the sitting posture, one hand is applied to the anterior part of the chest, the other to the posterior; in this manner the expansion is appreciated by the separation of the arms from each other. By examining alternately each half of the thorax and by seating one's self successively to the right and to the left of the patient, the deformities and expansion of each half may be determined with a little practice.

A procedure which is as simple as but more exact than the preceding consists in measuring each half of the chest with a centimetre measure, or even with a string. One end of the string being fixed at the spinous apophyses, the other end is brought to the middle of the sternum. In thus taking the measure, the modifications of

the thorax produced by breathing must, of course, be noted, and the degree of expansion at the end of inspiration and expiration registered.

Palpation.—Palpation practised with the hand flatly applied to the thorax at times reveals friction and râles. When there is abundant pleural collection it is possible to feel with the hands the fluctuation in an intercostal space. Palpation may also appreciate the beating and reducibility of certain tumours.

Palpation is particularly useful in recognising vocal fremitus. The patient is ordered to count aloud, and the physician, carrying his hands successively over all parts of the thorax, appreciates the intensity of vibrations, which may be increased, lessened, or absent. The changes are better noted when the two sides are compared. Increase in vocal fremitus indicates increased density of the pulmonary parenchyma; the phenomenon is therefore produced in case of compression, intense congestion, hepatization, and tubercular induration. Diminution of fremitus means that the parenchyma is rarefied, as occurs in emphysema, and especially that the lungs are abnormally separated from the chest wall; therefore fremitus is weak or altogether absent when the pleura is thickened, and particularly when there is liquid or gas in the sac. This research is one of great semeiological importance, for it serves to differentiate pneumonia from pleurisy and pneumothorax from a cavity.

Percussion.—After palpation, percussion is practised. Care should be taken to percuss from the apex of the chest downward, first in front and then behind, one side and then the other, and, moreover, to compare the two sides in percussing the homologous parts. It must be remembered, however, that sonority is not the same everywhere, even under normal conditions. On the right side there is an area of hepatic flatness appreciable behind and still more so in front, where it begins at the fifth rib and becomes absolute below the sixth.

The modifications of sound revealed by percussion consist in increase or diminution of sonority. In the former case tympanism is said to exist; in the latter, flatness.

Tympanism may be general, unilateral, or partial. When general, it corresponds to a permanent distention of the air cells—viz., to emphysema. It is unilateral especially in pneumothorax. When partial, it indicates a limited pneumothorax, or that the subjacent portion of the lung is pushed away and compressed. Hence, in case of pleural effusion and at times even of pneumonia, a tympanitic sound is often heard beneath the clavicle, designated as Skodism, in honour of a Vienna physician, Skoda, who demonstrated it.

Flatness may occupy a more or less extensive portion of one lung

or of both lungs. It varies in intensity. When it is very slight, as occurs in certain cases of tuberculosis, dulness is said to exist. Flatness is very obvious in pneumonia and is absolute in pleurisy.

Certain areas should be percussed with special care. These are the infraclavicular regions and the supraspinous fossæ. Dulness at the apex is, in fact, of great semeiological importance, since it is one of the principal signs of pulmonary tuberculosis.

A very careful percussion should be made over the roots of the bronchi in children. The ganglia located there, being often increased in size, give rise to flatness.

Finally, in the anterior and lower part of the left side, there is a semilunar space known as Traube's space, presenting tympanitic resonance with high pitch, due to the presence of the stomach. This space becomes flat on percussion in cases of very copious pleural effusion.

Care should always be taken to percuss during the two movements of breathing, directing the patient to open and close his mouth, and to sit down or stand up. In fact, it is readily understood that the tone should be more tympanitic during inspiration, for a greater amount of air is at this time present in the lungs. When the mouth is open, resonance increases; when it is closed, it diminishes. These modifications of resonance are supposed to possess diagnostic value in distinguishing a cavity from a pneumothorax; but, in reality, the differences are not constant.

In case of large cavities, the separate strokes of percussion below the clavicle elicit a peculiar sound, called cracked-pot sound (*bruit de pot fêlé*), which results from sudden compression of the air. This phenomenon is produced only when the mouth is open; it disappears after several percussions, to reappear after a deep inspiration.

It must also be remembered that the position of the patient modifies the results of percussion. The pitch is lower in the sitting than in the lying posture of the subject.

All these somewhat dry details are indispensable, since in a great many instances the differences appreciated by percussion are minute and have no value except when exploration is performed under well-determined conditions.

Auscultation.—Although percussion is very useful, auscultation affords information of greater certainty.

Auscultation, like percussion, should also be made from above downward, and the corresponding regions of the two sides compared. The points to be noted are the intensity and tone of the respiration, the relative duration of its various cycles, and in certain instances the superadded murmurs.

The breathing may be more intense than normally; then it is designated as puerile, for respiration is more active in children than in adults. It may be hardly perceptible or not all over a more or less extensive region: this is respiratory silence (pleurisy with copious effusion, massive pneumonia).

Modifications in pitch are very numerous. They are described as rude or harsh, humming or jerking, which terms sufficiently indicate their stethoscopic characters.

Finally, the relative duration of the various respiratory phases ·may also have been modified; notably expiration may become longer than inspiration.

These various modifications, though quite slight on the whole, acquire great importance in certain instances. Humming respiration, coinciding with exaggerated resonance on percussion, is a sure sign of emphysema. A jerking respiration with a prolonged expiration below the clavicle indicates incipient tuberculosis.

Superadded murmurs are of far greater importance. They are resolvable into frictions, which take place in the pleura, and râles, which are produced in the trachea, bronchi, or lungs.

It is not always an easy matter to distinguish *frictions* from râles. It is well to recall that frictions are more superficial and less regular, are generally heard at both phases of the breathing, and are not modified by cough. Their intensity and pitch are variable. At times they are slight and mild, similar to the murmur produced by the crushing of tissue paper; on other occasions they are intense, recalling the noise made by new leather. Their presence justifies the physician in diagnosticating a dry pleurisy.

Râles are resolvable into three groups: dry or sonorous râles, crepitant râles, and moist râles.

Dry or *sonorous râles* are called rattling when they have a grave pitch, and sibilant when acute. They are frequently intermingled and may coexist with a variety of sonorous râles resembling the clucking of the hen. They indicate bronchial inflammation or catarrh.

The *crepitant râle* is similar to the noise produced by throwing a little salt into fire; it may more exactly be obtained by taking a lock of hair between the thumb and finger and twisting it before the ear. This sort of râle is heard during or rather at the end of inspiration, and is characteristic of pneumonia.

Laennec described under the name of *crepitant râle of resolution* that sound which is audible at the third stage of pneumonia. It is clearly different from crepitant râle in that it is larger and moister and is commonly produced in both phases of the breathing. It is a subcrepitant râle.

Moist râles are divided, according to their size, into râles with gross bubbles, with bubbles of medium size, and with small bubbles.

Râles with gross bubbles, or *mucous râles,* are met with in bronchitis, in bronchiectasis, and in chronic pulmonary congestion. *Râles with bubbles of medium size,* or *subcrepitant râles,* are heard when the inflammatory process reaches the bronchi of middle calibre. *Râles with fine bubbles* signify capillary bronchitis, a focus of congestion, or incipient broncho-pneumonia. When located at the apex, they constitute a reliable sign of tuberculosis. When bubbling râles are mixed with sonorous or sibilant râles, a *tempestuous murmur* (*bruit de tempête*) is said to exist.

Cavernous is called a bubbling râle which gives to the ear the sensation of resonance in a cavity.

Unequal, irregular, dry, or moist murmurs are often heard at the apices, known as *crackling.* When dry, they are symptomatic of a beginning tuberculosis; when moist, they are connected with softening of the lesions.

There is *blowing* when the respiratory murmur is replaced by a sound more or less analogous to that which is heard on auscultation over the trachea or the roots of the bronchi. This stethoscopic phenomenon is due to condensation of the pulmonary parenchyma, which transmits to the ear the murmur produced in the adjacent healthy parts. The blowing is called *bronchial* when it is similar to that heard on auscultation of the bronchi. It is said to be *tubal* when it has a slightly metallic character. These various murmurs, whose qualities are very variable, may be well fixed in the ears by the following practice: The hands are united in the shape of an ear trumpet and through them the vowels *a, e, o,* or the diphthong *ou,* are pronounced in a low, blowing voice. By further narrowing the trumpet thus formed and pronouncing the vowel *i,* a different murmur is produced, which is analogous to the pleuritic blowing murmur.

The *pleuritic murmur* is a tubal blowing murmur transmitted from the bronchi to the ear through the lung compressed by the pleural effusion. The interposition of a liquid layer modifies the quality of the sound; the murmur becomes soft, as if veiled or produced at a distance from the ear. It is not absolutely distinctive of pleurisy, since it also occurs in certain pulmonary congestions, particularly in Grancher's spleno-pneumonia.

As to the bronchial murmur, it simply indicates increased density of the lung. It occurs under the most varied circumstances—e. g., pneumonia, broncho-pneumonia, pulmonary congestion, caseous masses, tumours, and sclerosis.

A murmur may be due, not to the transmission of a normal sound,

but to the production of a superadded one in some dilated or excavated portion of the respiratory apparatus. When dilatation is not considerable, a murmur similar to bronchial murmur is still heard, as is the case in dilatation of the bronchi. When, however, there is a large excavation, the *cavernous* or, at a more advanced degree, the *amphoric* murmur is met with. The former of these may be produced by blowing through the hands widely separated, the latter by blowing into a bottle with a large neck.

The cavernous or gurgling murmur is symptomatic of excavation, without, however, prejudging the pathological nature of the latter. It may be found in bronchial dilatation as well as in gangrene or abscess of the lungs, and by preference in tubercular cavities. It is often combined with moist râles which possess the same quality, and are designated, according to their size, as cavernular, or cavernous. When the râles are numerous and varied gurgling is said to exist.

The amphoric murmur, which at times originates in a vast cavity, is encountered especially in pneumothorax. In conjunction with it an additional murmur is very often heard, analogous to that which would be produced by grains of sand falling into a metallic cup: this is Laennec's *metallic tinkling,* due to the resonance produced through the layer of air by the fine râles in the lungs. The metallic tinkling should not be confounded with Trousseau's *brassy murmur (bruit d'aurain).* In percussing with one coin upon another flatly placed upon the anterior wall of the chest, a metallic sound is heard by auscultation of the posterior wall, which sound appears to be produced just under the listening ear. This is Trousseau's murmur of brass. Finally, as with air there is commonly associated a more or less considerable amount of liquid, it is possible, by shaking the patient, to hear a hydro-aerial noise similar to that produced when a half-filled bottle is agitated: this is *Hippocratic succussion.*

Lastly, the voice and the cough must be auscultated.

The patient should be instructed to speak aloud while the physician is auscultating. Sonorous syllables must by preference be pronounced. It is customary to tell him to count, beginning with 30, or to repeat the figure 33. The voice assumes the same quality as the murmur. Should a sharp and tremulous pleuritic murmur exist, the voice will also arrive at the ear with the same characters: this is *egophony.* This phenomenon is almost pathognomonic of pleurisy or of spleno-pneumonia; it is often more clearly heard than the blowing murmur. In cases in which bronchial or cavernous murmur is present, the voice partakes of the bronchial or cavernous quality.

Moreover, the whisper of the patient is in some instances perceived by auscultation as clearly as though the patient were speaking

into the ear: this is called *aphonous pectoriloquy,* which is mostly observed in serous pleurisy.

Those above indicated are the principal physical signs to be looked for in cases of pulmonary affections. In order to diagnosticate well, one must consider all the phenomena observed, coordinate and group them, and also take into account not only their characters but their locations. For instance, localization at the apex is an important sign of tuberculosis. Furthermore, the mobility of certain phenomena should not be overlooked. The stethoscopic signs are apt to vary considerably from one moment to another in uncomplicated bronchitis, particularly in pulmonary congestion, and at times in bronchopneumonia.

Not including emphysema and the rare lesions of the lungs, we can easily represent in tabular form (page 439) the diverse physical signs which enable the physician to make a differential diagnosis of thoracic diseases. It is of course to be remembered that the diagnosis is not possible unless the subjective disturbances, expectoration, general phenomena, and especially the course of the events are duly taken into consideration along with the physical signs.

Examination of the Digestive Canal

Examination of the alimentary tract must be made from above downward, beginning with the lips, teeth, tongue, and throat. Very little can generally be learned from observation of the lips, and what little information is obtained is not connected with the condition of the digestive organs. It will suffice, therefore, to recall here the dryness of the lips in grave infections, the trembling observed in a great number of nervous diseases (the most remarkable type of which occurs in general paralysis), the eruptions, such as herpes, which are produced in fevers, the bluish colour of cardiac patients, etc.

Examination of the *teeth* is of greater interest. In children, the delayed appearance of the teeth is dependent upon nutritive derangements. Their erosions and notches are symptomatic of rickets and hereditary syphilis. In the case of syphilis a lesion of great semeiological bearing is frequently observed, consisting in a peculiar form of the upper incisors, to which reference is already made under the designation of Hutchinson's tooth (page 228).

Dental caries possesses considerable importance; it sometimes explains digestive disturbances. Many dyspeptics have been cured by having their teeth taken care of, or by using artificial teeth. On the other hand, premature decay of the teeth is often referable to nutritive disorders. In diabetes, for example, the second lower molars are affected and their alteration serves as a guide to the diagnosis. Prema-

Percussion.	Palpation (Vocal Fremitus).	Auscultation.		Auscultation of the Voice.	Affections.
		Râles.	Blowing murmurs.		
Absolute flatness.	Absent.	Respiratory silence.	Respiratory silence.	Respiratory silence.	Very abundant pleurisy.
Flatness with skodism.	"	"	Soft, veiled, distant.	Egophony and aphonia, pectoriloquy.	Pleurisy with moderate effusion.
Flatness.	Generally absent.	A few crepitant.	"	"	Pulmonary congestion with pleural type (spleno-pneumonia).
"	Increased.	Fine subcrepitant.	Bronchial.	Bronchophony.	Pulmonary congestion with pneumonic type.
"	"	Crepitant.	Tubal.	"	Pneumonia.
Flatness or dulness.	"	Limited subcrepitant.	Limited bronchial.	"	Broncho-pneumonia.
"	"	Dry crackling.	. . . .	Resonance.	Tuberculosis (first degree).
"	"	Moist crackling.	. . . .	"	Tuberculosis (second degree).
"	"	Moist.	Bronchial or cavernular.	"	Small cavities or bronchial dilatation.
Flatness.	"	Cavernous râles and gurgling.	Cavernous.	Cavernous voice.	Generally tubercular cavities.
Flatness or tympany.	"	Gurgling.	Amphoric.	Amphoric voice.	Large cavities.
Tympany.	Absent.	Metallic tinkling.	"	"	Pneumothorax.
Normal sonority.	Normal.	Mucous.	"	"	Simple bronchitis.
"	"	Fine subcrepitant.	"	"	Capillary bronchitis.

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ture loss of the teeth must also be taken into consideration, since it reveals failing nutrition, and at times a nervous affection, such as locomotor ataxia.

Dental alterations often coexist with gingival lesions. The state of the gums should therefore be noted; they may be ulcerated or covered with a pultaceous exudate. When saturnine intoxication is suspected, examination of the gums is of great consequence, since the bluish line at the insertion of the teeth is absolutely characteristic.

Examination of the mouth is completed by that of the cheeks, where not infrequently are found ulcerations, pustules, and pigmentary spots, as occurs in Addison's disease. At the corners of the mouth are observed nacreous patches, called smokers' patches.

Examination of the Tongue.—The appearance of the tongue is of greater interest. In cases of digestive disorders, especially an attack of indigestion, the tongue is large, bearing the impression of the teeth, and often covered with a whitish or yellowish coating. It is dry in grave fevers, and becomes covered with a fuliginous, dark coating.

In certain diseases the appearance of the tongue is sufficiently peculiar to acquire a certain diagnostic value. In typhoid patients it is white in the middle and red on the borders. In influenza, according to Dr. Faisans, it presents the appearance of porcelain. Its examination is of especial service in scarlatina. When the eruption has disappeared or is not clearly marked, the diagnosis is made dependent upon the state of the tongue, whose mucous membrane, deprived of the epithelium, presents a set of papillæ of a deep red or raspberry colour.

Of the other alterations of the tongue we shall mention the pigmentary modifications and slaty patches of Addison's disease, the black deposits of parasitic origin, the desquamations in areas (marginate exfoliating glossitis, geographical tongue), which were unjustly attributed by Parrot to syphilis; the patches of tobacco smokers, and the white, corneous patches designated as leucoplasia or lingual psoriasis, which are unimportant of themselves, but are often transformed, in the course of a few years, into epithelioma.

Finally, ulcerations may be met with in the tongue. Some of them are simply caused by dental lesions; others are referable to some acute infection or to intoxication; and others are produced by syphilis, tuberculosis, and cancer.

The modifications of the saliva are more important. The secretion is diminished in acute infections and in certain poisonings (belladonna); in certain other poisonings it is increased (pilocarpine), in buccal inflammations, notably in gingivites, mercurial or ulcero-membranous stomatitis, in certain nervous diseases, and especially in dyspepsia. In the last-mentioned case the saliva, abundantly produced,

is swallowed during the night and accumulates in the stomach; in the morning, on awakening, the patient has a pituita whose salivary character is demonstrated by the presence of potassium sulphocyanide, tested by perchloride of iron.

The breath should not be overlooked, for it is often fetid, either by reason of increased fermentation in the alimentary canal, or owing to the presence of putrefactive lesions in the mouth or throat, or sphacelus in the bronchi or lungs. The volatile products which develop under the influence of microbes are absorbed and eliminated by the lungs as well as by the skin.

Examination of the Throat.—Examination of the throat, which is made simply by depressing the tongue with the handle of a spoon, should never be overlooked, especially in children.

The patient facing the light, the physician examines the palate, the uvula, the pillars, the vault of the pharynx, and the tonsils, care being taken to press the tongue well down when looking at the tonsils in order to get a view of their lower part. The motility of the soft palate and uvula, the colour and development of the various parts, the presence of ulceration and false membranes must be noted. In certain cases it is necessary to introduce the index or, better, two fingers into the mouth in order to determine whether a tonsillar ulceration represents an indurated chancre, or whether a pharyngeal tumefaction is due to a fluctuating abscess.

Throat inflammations assume two principal appearances. In some instances the mucous membrane is red, without any whitish exudate, as is the case with simple sore throat, either idiopathic or symptomatic, and at times with phlegmonous angina. In other instances the mucous membrane is covered with a whitish deposit. When the exudate is thick, slightly greenish-white in colour, adherent to the mucous membrane, uniformly spread, occupying both tonsils and invading adjacent parts, especially the uvula, then diphtheria must immediately be thought of. The moderate febrile reaction, the swollen glands, and, in some cases, the edematous tumefaction of the neck, the bad general state, and the paleness of the skin further help to establish the diagnosis of diphtheria. On the other hand, diphtheria is excluded when the exudate is white and limited to the tonsils, presenting small rounded patches disseminated in the tonsillar crypts, and attended by a sudden and intense rise of temperature, while the general state remains tolerably good. Then cryptic, herpetic, or simple membranous sore throat is said to exist. Finally, angina is called pultaceous when the exudate is thick, creamy, and loosely adherent.

There are also ulcerating and gangrenous anginas, but they are quite uncommon.

The differential diagnosis of anginas gives rise to serious difficulties. In fact, the following questions must be answered: Is the angina catarrhal, phlegmonous, pseudo-membranous, gangrenous, or ulcerating? Is it primary, or symptomatic of rheumatism, of erysipelas, or of mumps? Is it one that occurs in the beginning of eruptive fevers—i. e., measles, scarlatina, or smallpox? Is it a syphilitic angina? If a primary angina, what is its nature? Especially when pseudo-membranes are present, is the case one of diphtheria?

We can not sum up here, not even briefly, the differential characters indicated by authorities. Despite the minutest observations a great many clinicians at the present day believe that the diagnosis of anginas is impossible without the assistance of bacteriology. There is in this assertion one of those exaggerations of which the history of medicine furnishes so many examples. In the majority of cases the diagnosis can be made with a tolerable degree of certainty to satisfy the requirements of a rational treatment. However, in order to be able to make a clinical differentiation one must have examined a considerable number of angina cases and acquired an experience demanding far longer study than the bacteriological research of Loeffler's bacillus.

Examination of the Esophagus.—The lesions of the esophagus may give rise to marked disturbances of deglutition. An organic stricture or a reflex spasm produced by an ulceration, or compression exerted by a neighbouring tumour, especially by an aneurism of the aorta, causes the arrest of the alimentary bolus or its rejection by regurgitation or vomiting. In milder cases there is only a sensation of constriction.

The cervical part of the esophagus may be examined by palpation, which permits detection of tumefaction produced by accumulation of aliments in those cases in which the stricture is situated high enough.

Percussion exceptionally reveals an area of flatness at the sides of the spine. Gurgling in the dilated portions may be heard by auscultation. If the patient swallows water, it may be noted by means of auscultation that the noise which is normally heard all along the esophagus is not audible below the point of stricture.

All these procedures are generally insufficient. A more complicated examination and the use of catheterism are nearly always required in order to arrive at a positive diagnosis.

Examination of the Stomach and Intestine.—The digestive canal—viz., the stomach and intestine—is the source of disturbances which are as numerous as they are varied. As always, examination must first be guided by interrogation in the following manner:

The patient should be asked whether his appetite has increased, diminished, or been perverted, or whether he experiences disgust for

certain foods. In case of cancer of the stomach, the patient has an invincible disgust for meat.

He must next be questioned whether certain aliments or certain condiments render his digestion more troublesome. The influence of acid foods and those containing vinegar should particularly be inquired into.

Then the sensations experienced after meals should be noted. Disturbances may appear immediately or some time after taking food. Sometimes even before the end of a meal the disorders appear, such as a sense of discomfort and fulness, at times pain, or even vomiting. In other instances the trouble is felt from one to four hours after taking food. The symptoms are divisible into two main groups. There may be slow digestion with a sense of fulness and swelling. This is the hypohydrochloric type. Or there may be intense or even very violent pain, often in the form of cramps. This is the type of hyperacidity— i. e., there is excess of hydrochloric acid in the stomach. In order to confirm the diagnosis sodium bicarbonate should be administered at the time of pain. The hydrochloric acid thus being saturated by the base, eructations of carbonic acid are produced and the pain vanishes in a few minutes.

Then inquiry is made as to the other gastric phenomena. It should be learned whether the patient has morning pituite—which is so common in catarrhal gastritis, especially when it is of alcoholic origin— regurgitations, vomiting, or eructation; and in case the answer be affirmative, their characters, notably their odour, should be carefully ascertained. Then follows an inquiry into the condition of the intestine—whether there is constipation or diarrhœa, and what are the characters of the fæcal matter. Finally, the associated phenomena, especially the nervous manifestations, should be considered—e. g., headache, congestion of the face, somnolence after meals, insomnia during the night, a tired feeling, often more marked in the morning on awakening than in the evening, and inaptitude for work, all of which are symptoms of great importance.

Vomiting.—The vomited matters must be examined with particular care. Their quantity, consistence, and odour are at least approximatively noted. Their reaction is generally acid; it is alkaline in cases of catarrh and cholera. Then the variety of vomiting should be determined. Vomiting may be aqueous, alimentary, bilious, fæcal, hemorrhagic, or purulent.

Aqueous vomiting is represented by a colourless liquid, which is often viscid and ropy as a result of the presence of mucus or swallowed saliva. It is commonly observed in the morning in cases of alcoholic gastritis (pituita), ulcer, cancer of the stomach, in pyrosis,

and in cholera, where the vomited substances are remarkable for their resemblance to rice water.

Alimentary vomiting consists of foods and beverages more or less digested but still recognisable. This is the most common variety. Not infrequently the aliments are mixed with bile. When the latter is copious, it imparts to them an intensely green colour. These bilious vomitings are often observed in acute gastroenteritis, and especially in peritonitis.

Vomiting is said to be fæcal or fæcaloid when consisting of substances in appearance similar to those found in the intestine. This variety is of considerable semeiological importance; it is diagnostic of intestinal obstruction.

Vomiting of blood, or hematemesis, presents itself under two appearances. Sometimes the blood is red, sometimes dark, comparable to soot or coffee dregs. In the latter case the blood has sojourned in the stomach and been partly digested by the gastric juice. Dark-blood vomiting points decidedly to the existence of cancer; vomiting of red blood is observed in cases of ulcerating gastritis, and especially in simple gastric ulcer.

Finally, examination of vomited matters may reveal therein the presence of foreign bodies or parasites, notably ascarides. To this reference will be made in connection with microscopical examination.

The manner in which vomitings occur should also be taken into consideration. They may be preceded by nausea and attended by effort, as is the case with gastric vomiting. At other times they are produced after meals, occasioned by a particularly troublesome paroxysm of coughing, such as occurs in consumptives and in those suffering from whooping cough. Vomiting may sometimes take place by simple regurgitation without giving rise to any sense of discomfort. It is very important to be familiar with this variety; it is observed in cases of cerebral or meningeal lesions.

Fæcal Matters.—To appreciate the modifications of fæcal matters is no less important than the study of the varieties of vomiting. Under normal conditions a man evacuates daily 120 to 180 grammes of fæces, of a tolerably firm consistence and cylindrical form, of brown colour and very slightly putrid odour. They may therefore become modified in amount, character, form, colour, and odour.

The quantity diminishes in certain cases of incomplete constipation. Evacuation does take place, but less abundantly. The individual has from time to time copious evacuations which empty the bowels.

The consistence of the matters may also be increased or diminished. When hard, their form is also modified: they are at times reduced to small round masses, at others to thin ribbons, and also as though

passed through a wire-drawing plate—pipe-stem fæces. The latter is observed in cases of rectal stricture.

When the consistence is lessened, the matters are either simply pasty, or liquid, containing or not solid particles. Since diarrhœa is generally dependent upon increased intestinal putrefaction, the matters exhale an extremely fetid odour. This is not, however, true of all cases; in cholera the dejecta are odourless.

Whether diarrhœa be present or not, the colour of fæcal matters may have been profoundly modified.

In the first place, the influence of diet should be noted. In infants who take milk only, the appearance is that of a gold-yellow paste. When an adult is placed upon a milk diet and digestion is quite satisfactory, the fæces are dark in colour, hard in consistence, and in small rounded masses. As soon, however, as digestion becomes disturbed they acquire the nature of infantile fæces: they assume a pasty, yellow, or even whitish character.

The stools are colourless when the bile no longer contains pigment (Hanot's pigmentary acholia), and especially when it ceases to flow into the digestive canal. Hence the necessity of inquiring into, or rather personally examining, the state of the fæcal matters whenever hepatic disorders exist. The condition of the biliary passages is evidenced by the stools being coloured or colourless; in cases of icterus the colour shows whether there is polycholia or retention of bile.

The stools may be mixed with blood. The latter, as in the case of vomiting, appears under two forms: at times it is red, mixed or uncombined with excrement. In other instances it appears in the shape of blackish flocculi, comparable to coffee dregs; then *melæna* is said to exist.

The red blood, except when it is very abundant, proceeds from the lower portions of the large intestine or the anus. It is, therefore, necessary in such cases to carefully examine the anal orifice, and, by means of inspection and touch, to look for hemorrhoids.

Black blood may proceed from the stomach; it then makes its appearance in consequence of a hematemesis: otherwise it is referable to some intestinal alteration, some ulcerating process the nature of which should be determined in accordance with the other phenomena observed.

Melæna should not be confounded with the black colour produced by certain medicaments. In individuals who have ingested metallic salts which form insoluble black sulphides in contact with the sulphuretted hydrogen of the intestine, the stools assume a very dark colour. This occurs particularly after the ingestion of subnitrate of bismuth.

The colour of the alvine discharges is still more profoundly modi-

fied in cases of diarrhœa. In simple enteritis the colour is light brown, whitish or greenish yellow. In typhoid fever the evacuations are of a yellowish colour and nauseous odour. In catarrh of the large intestine they are made up of a yellowish liquid mixed with mucus; and the patient often expels, after a colic, small viscous masses of a rusty colour, recalling somewhat the expectoration of pneumonia. At a more advanced stage he expels true masses of glairy substance mixed or not with false membranes. This is particularly observed in dysentery: the patient each time evacuates very small amounts of slimy, reddish matters mixed with blood and fragments of mucous membrane; their discharge is attended by rectal tenesmus and often by dysuria.

There is another variety which consists of aqueous, colourless, diarrhœal matters containing ricelike epithelial *débris*. The best-known example of this is seen in cholera.

Finally, the stools, while as a rule diarrhœal, may present a whitish colour due to the presence of a great amount of fat. *Fatty stools* are of great diagnostic value; they indicate that the pancreatic juice no longer flows into the intestine.

Examination of fæces also reveals the presence of substances which are not normally met with.

Alimentary residue, at times even aliments which are discharged undigested, may be found in the stools. This phenomenon, designated as *lientery*, is symptomatic of an extensive alteration of the digestive mucous membrane, or of a fistula which, establishing a communication between two portions of the intestine far removed from each other, deprives part of the aliments of the action of the digestive juices.

There may also be found anomalous productions in the fæces—e. g., solid bodies—which, when voluminous, are readily perceived. If they are of small size they must be looked for by first throwing them upon a sieve and then placing them under a current of water. The substances will pass through the meshes and in the residue, apart from alimentary *débris*, will be found stony productions. Some of these have the appearance of sand and gravels and proceed from the intestine itself. Others have originated in the biliary passages, and are called hepatic calculi, easily recognisable by their yellow or green colour, smooth and polished surfaces, slight density, and high percentage of cholesterine.

False membranes, often found in the fæces mixed with mucus, occur under the form of lamellæ and ribbons, which are not infrequently confounded with tænia, and at times under the appearance of ramified tubes. The presence of these productions, due to desquamation of the mucous membrane, is of great semeiological value. It is

symptomatic of an intestinal affection extremely difficult of treatment—viz., *muco-membranous enteritis.*

Excrements frequently contain parasites. In most cases the patient himself finds them accidentally and reports to the physician. The latter must first verify the parasitic nature of the parasite. In this connection error is not uncommon. Pseudo-membranous fragments and even poorly digested aliments have been mistaken for worms. The nature of the worm is next to be determined. The ascarides are readily recognised. The ribbonlike worms present a series of characters indicated in every treatise on natural history, which readily permit of their recognition.

Finally, in a great number of instances the study of the discharges must be completed by a microscopical examination, in order to see things invisible to the naked eye—e. g., alimentary *débris*, parasites, and spores of bacteria.

Examination of the Stomach.—After having concluded questioning of the sick and examination of the excreta, consideration of the physical signs must be taken up, beginning with the stomach, continuing with the intestine, and ending with the glands annexed to the digestive tube.

Inspection.—In examining a stomach it is best always to begin with inspection, which reveals various deformities, which have been well studied by Dr. Hayem.

Deformities may be produced by the corset. There are three varieties of them. In some cases compression is suprahepatic, in consequence of which the organs are pushed downward. There is visceral ptosis. In other instances compression bears upon the liver and a strangulation is the result, the mark of which is found at the autopsy. Compression may also be infrahepatic; then, the viscera being pushed into the thorax, dyspnœa and, especially, palpitation are produced.

Apart from these particular cases, the patient facing the physician, four varieties of deformity may be seen: (1) An upper enlargement, occurring in great eaters; (2) an enlargement of the lower parts of the abdomen, which is met with in debilitated individuals, in women who have had several pregnancies, and in patients suffering from visceroptosis; (3) a median bulging, connected with gastric dilatation; and (4) a flattening of the epigastric region with a bulging of the hypogastrium, which indicate dilated stomach with depressed organs.

When the patient is turned to one side three deformities are noticed: (1) A substernal depression, depending upon an exaggerated vacuity of the stomach and observed in cases of inanition or after

repeated vomiting; (2) an epigastric bulging, connected with distention of the stomach; and (3) a subumbilical flattening with hypogastric protrusion, characteristic of visceroptosis.

Palpation.—Palpation, following inspection, recognises the sensitiveness of the viscera, and whether any of them have become painful or enlarged. Certain precautions, however, should be taken. The patient must lie upon the back, the head being very slightly raised, the mouth open, the thighs flexed, and breathe forcibly. The physician must warm his hands if they are cold; without this precaution, reflex contractions would be produced in the abdominal muscles, embarrassing the examination. Seating himself to the left of the patient, the examiner makes several little strokes with the three middle fingers held close together and slightly curved. In this manner two things are perceived—an auditory sound, called *clapotage*, comparable to that obtained by shaking a bladder half filled with water, and a tactile sensation, a shock of return.

A normal stomach should not give the murmur of *clapotage* six hours after meals, and when it is full of food the murmur in question should not be audible except over an extent of about 2 inches below the false ribs. The eliciting of *clapotage* during fasting may be negative even if there is dilatation, for the reason that the stomach is empty. It will then suffice to cause the patient to swallow a small amount of liquid for the distention to become apparent. It may be made more manifest if he be directed to drink a little Seltzer water.

It has justly been objected that this inquiry into *clapotage* exposes to certain errors. For example, a dilated transverse colon gives analogous murmurs. But the *clapotage* of the colon is heard farther below and is nearly always obtained in the adjacent parts of the ascending and descending colon. In this manner the course of the large intestine can be outlined and the *clapotage* distinguished from that of the stomach.

Palpation also furnishes other information. For example, the cancerous tumours of the stomach, at least those of the pylorus and greater curvature, can be felt by this mode of exploration, to which the tumours of the cardia and lesser curvature are not accessible. Moreover, in case there is simply a cancerous infiltration, a diffuse induration can be felt. The presence of tumefaction, however, does not necessarily indicate the existence of a cancerous growth. Noncancerous indurations of the pylorus are not absolutely rare, especially in the aged. Likewise, the borders of a gastric ulcer may be indurated and impart the sensation of a tumour, but the other symptoms are sufficiently different to permit of an easy diagnosis.

Percussion.—Percussion must be made lightly, with one finger at least below the false ribs. Above them more strength can be used. By this means a tympanitic space (Traube's semilunar space) is made out on the left side; its upper limit is represented by a line starting from the left border of the sternum, at the fifth interspace, and continuing in this space as far as the mammary region. From this point the line descends to the seventh rib at the level of the nipple and terminates at the eighth rib on the axillary line.

The lower limit evidently varies according as the stomach is empty or full. The sonority of an empty stomach is not heard beyond two or three fingers' breadth from the costal border; after meals it may be perceived at two fingers' breadth above the navel. The sonorous zone measures 10 to 14 centimetres from above downward; transversely, 18 to 21 centimetres. On the left it is limited by the splenic flatness and below by the tympany of the intestine, the quality of whose tone is quite different from that of the stomach.

Auscultation.—Auscultation of the stomach is of little consequence. The patient complains of anomalous noises; in the evening, when he is in the lying posture, he hears a glou-glou in his stomach on turning to one side or the other. These noises are of two kinds. Some are produced in an irregular manner and are due to gastric contractions; others are rhythmical, and are heard in the standing posture in women whose corsets are too tight. Dr. Hayem explains this by the bilobal shape of the stomach, and supposes that the gas passes from one pouch to the other with each respiratory movement.

Examination of the Intestine.—Examination of the intestine follows that of the stomach and is made nearly in the same manner. However, *inspection* renders but little service, except in cases of intestinal obstruction, when accumulation of gas above the obstacle produces partial deformities which point out the site of the lesion.

Palpation is resorted to in most cases. The painful points are first looked for. The most important is that of McBurney, indicative of appendicitis; it is seated at the middle of a line extending from the navel to the anterior-superior iliac spine: it is the point corresponding to the insertion of the vermiform appendix upon the cæcum.

In cases of muco-membranous colitis the pains are periumbilical, or they occupy the right iliac fossa and the angles of the colon; while in dysentery they are felt in the left flank, extending as far as the anus.

Palpation also detects tumours and indurations of the intestine, and the presence of scybala, which in cases of chronic constipation may be hard enough to simulate a true tumour. This mode of ex-

ploration is of very great importance in cases of obstruction and, especially, invagination, as it is possible to feel the sausagelike portion of the intestine, particularly in children.

There is an affection called *enteroptosis*, study of which is made by means of abdominal palpation. This morbid state is characterized by the prolapse not only of the intestine, but of all the abdominal viscera. Their means of support have become insufficient, and consequently all are displaced downward.

Glénard, who has made a remarkable study of this morbid state, thinks that a great number of gastric dilatations should be considered as cases of gastroptosis. It is therefore necessary to carefully look for organoptosis whenever gastric dilatation is observed. When such is the case, a hard cord is perceived above the navel, extending transversely. This is the colonic cord of the colon, which can readily be pushed upward, but which resists an attempt to push it downward; if force is used, it slides and ceases to be palpable. In the left side the cord of the ilium can be rolled under the finger; it lies parallel to the Fallopian arch; on the right side a compact and hard mass is felt, which is the cæcum full of fæcal matters, since most persons affected with enteroptosis are victims of habitual constipation. By continuing the palpation it is possible to determine, by procedures later to be described, that the liver is lowered, and that the right kidney has left its position and protrudes below the epigastric region.

The coexistence of renal ectopia and gastric dilatation has long been noted. Bartels thought that the displaced kidney compressed the duodenum, and thus obstructing the course of the contents, caused a dilatation above the point of compression. According to Bouchard, dilatation of the stomach is primary; it produces congestion in the liver, and this organ, assisted by a corset or a belt, pushes the kidney out of its normal position. Glénard assumes that a laxity of ligaments exists; he argues that the right colonic angle only is affected first, and that the kidney is subsequently drawn out by it.

Finally, there is a mode of exploration which renders some service in the diagnosis of visceral ptosis. In case the patient is attacked with abdominal suffering, in order to relieve him it will suffice to raise up the viscera. To this effect, the subject is instructed to assume the upright position; the physician stands behind him, and, pressing above the pubis, with his two hands joined at an angle, he pushes the viscera from below upward: this procedure produces immediate relief. Exploration is then complete; all that is needed is to prescribe a belt which will compress in the same manner and tend to bring the organs to their normal position.

Examination of the Peritoneum.—The palpation practised for the intestine recognises at the same time the state of the peritoneum. The inflammatory lesions of the serous membrane, or even of the organs covered by it, increase its sensitiveness considerably. Palpation then becomes painful and gives rise to reflex contractions, a sort of defensive movement, in the abdominal muscles. This phenomenon is an important sign of peritonitis, appendicitis, and, in case of traumatism, should suggest a visceral lesion.

The acute or subacute inflammations of the peritoneum may likewise be very painful. In tubercular peritonitis palpation is generally very troublesome. In some instances, however, after having strongly compressed the wall, the hand must be removed abruptly in order to arouse pain. Finally, it is well to know that even acute peritonitis may be painless, and without any appreciable local reaction. In such cases acquaintance with the antecedent history and a minute study of concomitant manifestations will enable the physician to arrive at a diagnosis.

In chronic, and especially in tubercular peritonitis, palpation reveals hard or resisting parts and pasty masses, and at times it furnishes peculiar sensations compared to the sound produced by crunching snow. Finally, it reveals the presence of a hard cord extending from one side to the other of the abdomen across the navel; this is the great omentum infiltrated and retracted.

In rarer cases of peritoneal cancer an infiltrated mass or a set of small separate tumours, at times movable, escaping under the pressure of the fingers, are met with. This examination is sometimes rendered difficult by the presence of a peritoneal effusion.

It is readily understood that ascites causes distention of the abdominal cavity. If the walls are resistant, it produces an anterior protrusion, further exaggerated at times by the prominence of the umbilicus. Later on the walls yield and the fluid accumulates in the sides of the abdomen. Inspection thus reveals a deformity which becomes almost characteristic when dilated veins appear upon the abdominal wall, indicating obstruction of the deeper circulation. In order to establish with certainty the existence of fluid, percussion is resorted to, which elicits flatness in the lower portions, where the liquid has accumulated. When the patient is lying upon his back, a zone of flatness is found across the median line, on both sides of the abdomen, limited above by a tympanitic line with a superior concavity. The patient being instructed to alternately lie on the right and on the left side, the liquid is easily displaced, except when it is encysted by pseudo-membranes. It is well, however, to be acquainted with the fact that, even in cases of abundant ascites, a sonorous zone

is nearly always found in the posterior parts of the flanks, which is due to presence of the colon.

When the liquid is not copious the patient is advised to lie upon one side or to assume the knee-chest position; accumulation then takes place in the flank or at the umbilical level, and is expressed by absolute dulness.

The data of percussion are completed by looking for the succussion wave. The patient lying upon his back, the palm of one hand is placed on the side of the abdomen, and, tapping lightly with the fingers on the opposite side, waves are produced. Care should be taken, however, to prevent the transmission of the vibrations of the walls by having an assistant place the radial edge of his hand vertically on the median line while percussion is made.

It is very important also to discover whether the fluid is free or encysted. For this purpose the patient must be percussed in various postures. It must be noted whether the fluid flows from one side to the other when the patient turns upon his side. It follows the laws of gravity if it is free, whereas, if encysted, it presents no modification. The same exploration, completed by digital examination of the vagina, leads to the differential diagnosis between ascites and an ovarian cyst. In the latter case a liquid tumour exists, but it is situated laterally and can not be displaced, and it is furthermore limited by a line with inferior concavity.

The state of the mesenteric glands may also be examined by palpation. In children their tumefaction is particularly easy to appreciate, especially when they are invaded by tuberculosis. This affection was formerly designated as *carreau* or *tabes mesenterica*.

Finally, arterial pulsations are often perceived by palpation in the epigastric region, somewhat to the left of the median line. The patient sometimes calls the physician's attention to this point; he experiences palpitation in the stomach. Does this sensation depend upon dilatation of the aorta? It is natural to suppose so, for the pulsations are very superficial and auscultation often recognises there an intense diastolic murmur.* This symptom, which is mostly encountered in dyspeptic patients, and in those suffering from chronic enteritis and neurasthenia, should be well understood in order to avoid being led to the diagnosis of aneurism of the aorta or of the cœliac axis. This error is avoided by examining the patient several days in succession. These arterial palpitations vary from one day to another, and the physical signs to

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* The diastolic arterial murmurs are those produced during the dilatation of the vessel ; they therefore correspond to the cardiac systole or, more exactly, they follow it very closely.

which they give rise are correspondingly modified with the digestive disorders.

In abdominal exploration palpation renders the greatest service. Percussion reveals the state of the large intestine, whose tympanitic sound differs from that afforded by the stomach or the small intestine. It also serves to reveal the presence of abdominal tumours and intraperitoneal effusions. As to the rôle of auscultation, it is a limited one: it does no more than recognise certain intestinal murmurs or peritoneal frictions.

EXAMINATION OF THE LIVER.—Examination of the abdomen should be completed by that of the liver, spleen, pancreas, and kidneys.

Hypertrophy of the liver may be appreciable to mere inspection. A vaulting is noticed in the right hypochondriac region. When hypertrophy of the spleen coexists, as is not infrequently the case, then a tumefaction of the upper half of the abdomen is observed, especially in the standing posture. It should be borne in mind, however, that the liver is relatively far more developed in children than in adults, and even in a normal state causes a certain degree of vaulting.

In order to exactly determine the volume of the liver, both percussion and palpation must be resorted to. The patient being upon his back, the legs and thighs well flexed so that the abdominal muscles are relaxed, the physician places himself to the right and palpates from below upward and feels the lower border of the gland.

Percussion affords better information. It is made from above downward, and often it suffices to percuss on the nipple line; under normal conditions absolute flatness begins two fingers' breadth below the nipple and terminates at the costal border. The liver is therefore considered as prolapsed when its flatness begins and ends below these limits, and as hypertrophied when the upper limit of flatness is normal or raised and the inferior limit is lowered. These rules will often suffice. It is well, however, to be more precise and determine the whole extent of the flat zone. The upper limit is normally represented by a line beginning at the right border of the sternum, at the level of the sixth costal cartilage; it follows the sixth rib to the right mammary line, reaches the seventh rib on the axillary line, the ninth on the scapular line, and terminates near the spine at the level of the eleventh rib.

While strong percussion is needed to determine the upper limit of the liver, light percussion will suffice to mark out the lower limit. Without this precaution hepatic flatness would be masked by the sonority of subjacent organs.

Normally, the lower limit of the liver is confounded behind with

renal flatness: on the scapular and axillary lines it corresponds to the eleventh rib; then it follows the costal border, at equal distance from the ensiform cartilage and the umbilicus, and terminates on the left side at the level of the apex of the heart.

There are conditions under which hepatic flatness diminishes while the dimensions of the organ are normal. This occurs, for example, when there is pulmonary emphysema, gastrointestinal tympany, or when the intestine is pushed up by ascitic effusion.

Atrophy of the liver is observed in various morbid states, especially in atrophic cirrhoses, and in that morbid process designated in France by the clinical name icterus gravis, and in Germany by the name acute yellow atrophy.

Hypertrophy of the liver may be *general* or *partial.* It is general in biliary hypertrophic cirrhosis, in alcoholic hypertrophic cirrhosis, in fatty hypertrophic cirrhosis, and in the liver of heart disease and of amyloid degeneration. It is partial in cases of tumours, cancer, and hydatid cyst. Certain portions of the liver may atrophy while certain others become hypertrophic; this is observed particularly in syphilis. It is an important fact that partial hypertrophies of the liver are far more frequent than is believed. In a great many cases of cirrhosis one part of the gland develops to such proportions that the idea of an hydatid cyst is suggested. In not a few such instances laparotomy has been performed, and not until after the abdomen had been opened was the error recognised.

When the limits of hypertrophy of the liver have been exactly recognised by percussion, palpation must again be resorted to. The inferior border must once more be explored to determine whether it is sharp or rounded, resistant or soft. The surface must be examined with special attention in order to feel the small granulations in cirrhosis, and the voluminous nodes in case of cancer. Finally, inequalities, prominences, depressions, and fissures are perceived in syphilis; hence the characteristic name of *foie ficelé* (liver tied with twine) given to this alteration.

At other times a fluctuating tumour is felt, referable to a superficial hydatid cyst, and in certain rare instances a peculiar vibration is perceived by light percussion, which is known as *hydatid thrill* or *fremitus.*

Palpation sometimes appreciates pulsations isochronous with the pulse. In some cases they are nothing more than pulsations transmitted by the aorta. In other instances there is total dilatation of the organ, due to backward flowing of the blood at each ventricular systole. This is what is called the *hepatic pulse*, indicated by Sénac, well studied by Friedrich, and especially by Mahot. This phenome-

non, which is observed in cardiac patients at the stage of asystole, is to be sought for in the following manner: The palm of one hand is placed upon one side of the liver, the other on the opposite side; it is possible to thus perceive that the beatings are not transmitted; at each cardiac systole the liver becomes distended and pushes the two hands apart.

Exploration of the liver is not completed until the *gall bladder* is also examined. When it is distended, it is readily felt to the right of the rectus abdominis as a spherical or elongated tumour with resistant and hard walls, as if calcified. This biliary tumour is at times observed in lithiasis—less frequently, however, than might be supposed, since the cholecyst soon atrophies. The distention is more remarkable in an affection of difficult diagnosis—viz., cancer of the head of the pancreas. The patient is attacked by a jaundice which, as a rule, grows worse, or at least never recedes. At the same time emaciation and digestive disturbances are observed, and a characteristic hard tumour is revealed on palpation in the place of the gall bladder. If, moreover, the fæcal discharges, which are colourless in all cases of jaundice, are very rich in fat, cancer of the caput of the pancreas may confidently be diagnosticated. At any rate, aside from cyst of the pancreas, this is the only disease of this gland recognisable by our procedures of investigation.

EXAMINATION OF THE SPLEEN.—The main procedure applicable to the exploration of the spleen is percussion. It is made along a vertical line extending from the axilla to the left anterior-superior spine of the ilium. Under normal conditions the zone of absolute dulness extends from the eleventh rib to the lower border of the ninth and presents a length of about 5 centimetres. Splenic flatness is confounded posteriorly with that of the kidney.

In cases of considerable hypertrophy the spleen is appreciable not only to percussion, but also to inspection, and still better to palpation. This last mode of exploration also reveals the consistence of the organ, and the fluctuation observed in cysts and abscesses, as well as the unevenness of surface encountered in cancer.

Auscultation, which is of little importance in abdominal affections and serves only for the detection of peritoneal frictions, sometimes reveals a systolic murmur in cases of splenic hypertrophy.

EXAMINATION OF THE URINARY APPARATUS

Subjective Symptoms.—The first part of the examination of the urinary apparatus also consists in interrogation of the patient. The phenomena of pain are first to be inquired into, then the manner of micturition, and, lastly, the character of the urine is to be determined.

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Pain is felt in the lumbar and vesical regions. Lumbar pain is connected with lesions of the kidneys, the pelves, or ureters, and in most cases irradiates to the bladder. The pain may be dull and continual, or intermittent and paroxysmal.

Vesical pains are felt during micturition, and are especially marked when the last drops of urine are expelled, whereas, in case of urethral inflammation, the first drops give rise to the phenomenon of pain. It is also to be remembered that there may be renal or vesical pain without any alteration in the urinary passages. Such is the case with a great number of nervous diseases. Furthermore, if not pain, at least a certain burning is experienced during micturition when the urine is concentrated.

Apart from pain, disturbances of sensation in the urinary passage may be observed, dependent upon nervous diseases. In locomotor ataxia the patient does not feel the need of micturition; he satisfies this function by reason only, as he understands that the call must be attended to at certain intervals. Finally, in certain instances the urine is voided without causing any sensation, and, if the subject does not look at it, he does not know that he is urinating.

Some patients are otherwise annoyed. They frequently feel like passing water and are compelled to satisfy this feeling at very short intervals. This trouble may be of a nervous origin, or may be connected with an inflammation which renders the bladder irritable and prevents it from becoming distended; it may also be dependent upon a chronic nephritis. It is well to add that *pollakiuria*, or frequent desire to micturate, is not necessarily associated with *polyuria*, or increased quantity of the urine.

The manner of micturition is also to be considered. The patient should be questioned whether he easily passes water and whether the jet has preserved its normal power; whether the length of the stream has not for some time been diminished; whether the liquid, at its issue from the urethra, is not divided into two jets or is not twisted, and whether, after micturition, he does not wet himself by a few drops of urine flowing an instant after. These various changes in micturition are highly important from a semeiological standpoint, as they point to urethral stricture. In certain instances the flow of urine is suddenly interrupted as the result of a transitory obstruction caused by a calculus.

Finally, two other and far more troublesome disturbances consist in the impossibility of emptying the bladder, or of retaining the urine, known respectively as *retention* and *incontinence*. Retention of urine is different from *anuria*. The former is characterized by lack of excretion and consequent distention of the bladder by retained

urine; whereas in case of anuria secretion is suppressed, and the bladder is therefore empty.

Examination of the Urine.—The patient is often aware of the quantitative variations of his urine; he recognises polyuria more particularly, which necessitates frequent and copious micturition, even during the night. The patient should, nevertheless, from time to time be instructed to collect all his urine passed in twenty-four hours. According as the quantity is found to be below or above 1,200 to 1,500 grammes, oliguria or polyuria respectively is said to exist.

Clinically, examination of the urine is of serious import. In order, however, to obtain useful information from this source, examination must be made by means of certain reagents. It is absolutely necessary to look at least for albumen and sugar. This analysis will be referred to in connection with the clinical application of scientific procedures. It will suffice here to indicate simply those modifications which can be recognised without the assistance of apparatus.

The odour, density, colour, transparency, and sediments of the urine, as well as its quantity, must be noted.

Normal urine has a peculiar well-known *odour*. Under pathological conditions the odour may become ammoniacal, which indicates a process of intravesical fermentation. Fæcal odour is due to the existence of a vesicorectal fistula establishing a communication between the rectum and the bladder. In diabetes the urine, like the breath, may often assume an aromatic odour, recalling that of chloroform. This phenomenon is of high diagnostic importance, since it is one of the first symptoms of the grave state already detailed as diacetemic coma (page 208). It is also to be remembered that the urine may present various odours after administration of drugs—e. g., oil of turpentine imparts to it an odour of violet.

The *consistency* of the urine is often modified; it is sometimes very fluid, sometimes thick, ropy, and viscid. It may very easily become frothy; then albumen must be suspected and sought for. Finally, it may fall upon the clothing and leave a deposit of glucose. It is well to know that this deposit attracts flies, and when these insects are seen to assemble in great numbers upon the trousers and shoes as soon as the patient lays them aside, diabetes should immediately suggest itself.

The variations in the *colour* of urine are highly important. It may be very pale, as is particularly the case when the amount of urine is increased in diabetes, interstitial nephritis, nervous polyuria, and at the time of urinary crises.

The colour is deep under reverse conditions, as realized by most of the infectious diseases, in which instances the urine is scanty,

reddish, and sometimes brown. In this last case the colour is gener-
ally due to the presence of urobilin, which may be recognised by
spectroscopic examination.

If the colour of the urine is intensely red, the presence of blood,
or at least hemoglobin, must be thought of. The spectroscope reveals
the latter substance, and the microscope the red blood corpuscles.
When the urine contains blood, the origin of the latter must be dis-
covered. In women, menstrual blood is mixed with the urine; it is
easy to avoid error in this connection. If the hemorrhage occurs
within the urethra, it generally continues, even when no urine is
passed; at all events it colours but the first drops of urine. It is
therefore well to instruct the patient to pass urine in several recep-
tacles, and then to make a comparative examination of the several
specimens. In cases of renal hemorrhage the blood is, as a rule, more
copious and is more uniformly mixed with the urine. When there
is a lesion in the pelvis or ureters, fibrinous casts are commonly found
moulded in these parts. Vesical hemorrhage is characterized by the
fact that the blood comes at the end of micturition with the last
drops of the urine.

Instead of being red, a bloody urine may present a brown hue as a
result of transformation of its colouring matter. It is then difficult
to differentiate it from icteric urine; in such cases Gmelin's test,
which will subsequently be mentioned, should be resorted to.

When questioning can not elicit the desired information, recourse
is to be had to certain simple tests to determine whether the colour
of the urine is due to the elimination of some medicine. Carbolic
acid, for example, imparts to the secretion a blackish-brown colour;
logwood, senna, and rhubarb colour it red; santonin renders it green-
ish yellow. Finally, the urine of patients affected with melanotic
tumours presents a black colour, especially when it remains for a few
hours in contact with the air.

Instead of being clear and limpid, urine is white when it contains
emulsified fat (*chyluria*) or pus. In the latter case a mass of viscous
consistence is deposited at the bottom of the vessel containing the
urine.

A urine which is limpid at the time of voiding may produce a
deposit when it cools. The sediment may consist of mucus in floc-
culent masses, or of urates which, after clouding the liquid, subside
in the shape of a red or rosy sediment. In other instances oxalates
or phosphates are found; the latter are dissolved by acetic acid.
It sometimes happens that these various mineral salts are deposited
within the bladder and are discharged as minute calculi, passage
of which through the urethra is generally attended by intense pain.

Apart from the deposits above indicated, the urine often contains urethral filaments which occur, as a rule, in individuals having a history of gonorrhœa. In certain cases it may even contain tissue *débris*, caseous products, and parasites proceeding from the urinary organs or even from the digestive passages.

We can not enlarge upon all these points, notwithstanding their great diagnostic value. The study of the urine, in reality, should never be passed over; it affords the physician indications of the highest importance.

Examination of the Kidney.—Examination of the urinary apparatus must begin with the kidneys. First of all the region is inspected. The patient should lie upon his abdomen, and in difficult cases he should assume a posture in which the light falls upon him from before backward. The physician, seated behind the patient, will then be able to appreciate whatever depressions and eminences exist. The subject should then be directed to turn upon his side, when a zone of absolute dulness, extending toward the axillary line, and perhaps beyond it, will be found on percussion. The information furnished by this mode of exploration, however, is far less important than that obtainable by palpation.

The subject lies on his back, the abdomen relaxed by flexion of the thighs and legs, and the physician places himself on that side which he wishes to examine. He first makes a bimanual exploration: he places one hand posteriorly upon the loins, while the other is applied anteriorly. By gradually pressing with the hand in front, and in doing so profiting by each expiratory movement, it is possible to palpate the kidney, at least when it is enlarged or has become movable; it is then readily sent from one hand to the other. In some rare cases resistance and even fluctuation can be appreciated.

In case of renal ectopia Glénard advises depression of the abdominal wall with the hand placed below the ninth rib. The other hand lays hold of the lateral part of the abdomen so as to squeeze it between the thumb and medius. The hand thus placed may, at a given moment, seize the kidney, which is being pushed toward it.

It is often a difficult task to find the kidney when the organ forms an enormous tumour protruding at the umbilicus and compressing the adjacent organs. It may even occupy one entire side of the abdomen, as occurs in cases of hydronephrosis, cancer, and sarcoma of the kidney, of such frequent occurrence in children.

Examination of the Bladder.—The bladder is explored by palpation and percussion above the pubis. When it is distended by urine, it is felt as a globular, hard, and absolutely dull mass. In this man-

ner certain tumours may be perceived. But the examination must then be completed by a rectal or vaginal palpation, which alone permits exploration of its fundus.

EXAMINATION OF THE GENITAL APPARATUS

We shall not dwell upon the examination of the genital apparatus, which is subject to a somewhat particular technic. We shall confine ourselves to indicating the main points.

In man, inquiry is to be made as to the sexual power, which is at times increased at the beginning of certain nervous diseases, but generally diminishes at a more advanced stage. Anaphrodisia is viewed unfavourably by most patients except diabetics. This minor detail is not without a certain importance.

The patient must also be asked whether he has suffered from previous affections, particularly gonorrhœa and other venereal diseases, and whether he is annoyed by any present trouble, such as spermatorrhœa, the frequency of which has been greatly exaggerated. It not infrequently happens that patients are worried by some phenomenon of an absolutely physiological order. For instance, in continent men defecation expels a certain amount of semen through the urethra by compression upon the seminal vesicles.

Examination of the penis reveals the existence of defective conformation, such as epispadias or hypospadias, which represent as many stigmata of degeneration. Cicatrices are often found upon the organ; it is well to remember, however, that the lesion most important from a semeiological standpoint—viz., the hard chancre—generally heals without leaving any trace. The soft chancre is followed by a loss of substance which is often quite deep.

Eruptions, eczema, herpes, syphilitic papules, or mucous patches (*plaques muqueuses*), and sometimes even tumours are found upon the penis or scrotum. Another important point to look for is a slight mucous or mucopurulent discharge (weeping penis), sequel of a long-extinguished gonorrhœa.

Palpation appreciates the state of the testicle, epididymis, and the part neighbouring the deferent canal. In palpating the scrotum attention should be directed to ascertain whether or not an inguinal hernia exists. The index finger having been introduced into the canal, the patient is told to cough; if there is hernia, a shock is perceived. Finally, digital examination of the rectum reveals the state of the prostate and seminal vesicles.

In woman, attention is to be first directed to menstruation. The points to be noted are: the epoch at which the function was established; the regularity or otherwise of the periods; the quantity and

duration of the flow; whether it is attended by pain, or the expulsion of clots or false membranes; and whether there are any general disturbances coincident with menstruation. Investigation is next to be made as to leucorrhœa—whether it is intermittent, becoming manifest shortly before or after the menses: in that case it is hardly of any consequence. In other instances a discharge has appeared and persisted, which, at first greenish, has gradually become more abundant and mucoid; this evidently suggests gonorrhœa. At other times the discharge is more tenacious and glairy; it originates from the uterus. The odour of the discharges is also of considerable importance. For instance, the fetid odour of the reddish discharge of cancer is characteristic.

The patient is to be questioned also with regard to the number of pregnancies, and whether any abortion or premature birth has occurred, and, a point of particular interest, whether they occurred with or without cause and whether they occurred repeatedly. Repeated abortions otherwise unexplained must be attributed to syphilis.

Examination of the external organs may reveal various eruptions, such as eczema, herpes, and syphilides. A chancre, hidden by some fold, may have remained unnoticed by the patient. The presence of inguinal adenopathia leads to the diagnosis of, or at least to an examination of the vulva for, a chancre. In other instances simply tumefaction is observed, œdema of the parts due to some inflammatory lesion of the vulva or vagina; or a unilateral tumefaction connected with an affection of Bartholin's gland; less frequently tumours are met with. The state of the urethra requires close attention, since gonorrhœal discharges are not so readily recognised in women as in men.

The more deeply seated parts are explored by palpation, which recognises cysts of the ovaries, the gravid uterus, or one affected by tumours, especially fibromata. It is necessary, however, to make at the same time a digital exploration of the rectum and vagina in order to well determine the state of the vagina, uterus, Fallopian tubes, and ovaries. In the majority of cases this exploration should be completed by an examination with the speculum.

EXAMINATION OF THE NERVOUS SYSTEM

Of all the organs and apparatus of the organism there remains only the examination of the nervous system. This last part of clinical research is particularly long and delicate, requiring especial knowledge. We shall therefore be content to indicate the principal rules which must guide the physician.

As has already been mentioned when treating of facies, in certain

cases the attention is immediately drawn to the existence of some nervous disorder. Paralyses, atrophies, and spasms impart to the countenance very peculiar appearances. Intellectual derangements impose upon it a special expression which can not escape the attention of a close observer.

MOTILITY.—The state of motility is, as a rule, examined first. According as it is diminished or suppressed, *paresis* or *paralysis* is said to exist. Paralysis of one limb is called *monoplegia*; that of upper and lower extremities of the same side, with or without participation of the face, is designated as *hemiplegia* or unilateral paralysis. Hemiplegia is said to be *crossed* or *alternate* when the face of one side and the limbs of the opposite side are involved. When the two superior or, what is a rare occurrence, the two inferior extremities are affected, there is *paraplegia*. Finally, the term *partial* or *limited paralysis* is employed if loss of movement bears upon a territory of limited extent.

Paralysis is readily recognised when it is well marked. All motion is suppressed in the affected part. When it is raised it falls again like an inert mass on being released. In slighter degrees of paralysis the affected part is still capable of executing certain motions, but such motions are embarrassing and incomplete. For example, a patient moves a paralyzed lower limb, but he is incapable of lifting the heel from the bed; or he can raise his arm, but is unable to place it over his head. It is therefore necessary to push the analysis further and not be content to note the paralysis; the degree of the latter should be ascertained and the muscles involved in the process determined. Paralysis of a limb can generally be recognised without difficulty. It will suffice to impart to the limb a certain passive motion and to ask the patient to resist it with all his strength, or simply to test the strength of his hand grasp. To investigate the state of the muscles of the thenar eminence, the following procedure is resorted to: The patient is asked to strongly press the thumb against the index finger; then a pencil is introduced into the ring thus formed and pushed so as to separate the fingers. Under normal conditions the pencil will meet with considerable resistance, while in a pathological state the fingers will be separated immediately.

The face must be examined first by a careful inspection. Paralysis, by effacing the folds, imparts to the face a marked asymmetry, which is further exaggerated by the contraction of the antagonizing muscles of the healthy side. The patient will be asked to execute grimaces alternately with each side, to blow, to whistle, to wrinkle the forehead, and to open and close his eyes. This last investigation is of great importance, for in cases of facial paralysis the participation or integrity of the *orbicularis oculi* is one of the best elements of diagnosis as to

whether the lesion is peripheral or central. The orbicularis is spared when facial paralysis is due to a cerebral lesion. It is involved in the contrary case, and then closure of the eyes becomes impossible.

Finally, the patient will be asked to put out his tongue, when the tip will be deviated to the affected side, owing to the action of the genio-glossus of the healthy side.

The affected muscles may be relaxed or rigid. In the former case paralysis is said to be *flabby*; in the latter, that it is attended by contracture.

Contracture.—Whether consecutive to paralysis or not, *contracture* is essentially characterized by involuntary and persistent rigidity of certain muscles. The muscles thus affected are hard, and their elasticity appears to be diminished. When an attempt is made to modify the situation of the diseased part a peculiar resistance is met with. Contracture is frequently accompanied by two phenomena of importance to be referred to later on—viz., exaggeration of reflexes and epileptoid trepidation. Contracture sets in generally in consequence of a traumatism, and disappears during chloroformic sleep or after a prolonged application of an Esmarch bandage.

Contracture may assume a hemiplegic, a paraplegic, or a partial form. Although in the majority of instances the antagonizing muscles are affected, the predominance of certain groups gives rise to a peculiar position: thus a type of flexion is mostly observed in the superior extremities, while a type of extension generally occurs in the lower. The arms stick to the body, the forearm is flexed at a right angle, the hand in flexion and pronation, and the fingers forcibly closed. In the extension type, the forearm is extended while the fingers are flexed. In the inferior extremities the several segments are in extension, except the toes, which are flexed toward the sole of the foot.

Of partial contractures we shall cite only the glosso-labial hemispasm of hysterical patients, long confounded with facial paralysis.

Contracture may be due to hysteria, or be directly or indirectly caused by an inflammatory or painful lesion, or connected with some affection of the brain, spinal cord, or meninges. All cerebral lesions reaching the pyramidal tracts sooner or later give rise to contracture. When the latter appears at an early stage it is dependent upon simple irritation; when occurring at a later period it is the product of descending degeneration. Of central diseases it will suffice to mention encephalitis, hydrocephalus, tumours, hemorrhages, and softening of the brain; of medullary diseases, myelitis, multiple sclerosis, lateral amyotrophic sclerosis, and tabes dorsalis spasmodica. Meningitis also counts contracture among its symptoms. When this symptom is

absent, it may be aroused in the following manner: The patient is requested to sit upon the edge of the bed; it is then found that it is impossible to extend the knees as completely as when in the lying posture: this is known as Kernig's sign.

The true contractures are not to be confounded with certain muscular rigidities, designated as pseudo-contractures, which are observed in paralysis agitans, pseudo-hypertrophic paralysis, and myopathic atrophy. In this case the antagonists are not affected, the reflexes are not exaggerated, and chloroform can not dispel the rigidity.

Gait.—When a patient is affected by a paralysis or a contracture which, although involving the lower extremities, still permits the subject to walk, a series of disturbances are observed the investigation of which is of great semeiological importance.

In case of flabby hemiplegia, and more particularly in hysteria, the leg is dragging: this is the *helcopode* (ἕλκειν, to drag) gait. The sole of the foot sweeps the ground. If a certain degree of spasm also exists, as occurs in organic hemiplegia, the gait is *helicopode* (ἕλικος, circular movement); the affected limb describes a half circle and comes in contact with the ground by the toes.

With a flabby paraplegia the patient takes short steps with the legs widely separated. He alternately drags each of the inferior limbs without lifting them from the ground. At each step the pelvis executes alternate movements of inclination and rotation.

The spasmodic gait of paraplegia with contracture is characterized by slow and short steps. The feet are raised with difficulty from the ground upon which they rest with the toes alone. At each step they turn inward, tending to cross each other; the knees touch and the thighs are closely approximated; finally, the trunk inclines alternately to the right and to the left, executing real balancing movements (cross-legged progression).

The same manner of gait is observed in paralysis agitans, except that in the latter there is an additional feature—viz., an irresistible tendency to precipitate the movement—some sort of propulsion which has given origin to the saying that the patient appears to be pursuing his centre of gravity. By drawing him backward, retropulsion is obtained.

In cases of peripheral neuritis *steppage* is observed. Paralysis of the extensors, especially of the triceps and the anterior and external muscles of the leg, causes the toes to drop; the patient is obliged to raise the leg too high, and the knee being incapable of extension, he must strongly flex the thigh upon the pelvis; the toes that remain pendent then reach the ground first. This manner of gait, which is sometimes described as *pseudo-tabes*, is observed especially in polyneu-

rites of alcoholic, saturnine, and diabetic origin. It is totally different from the gait of true locomotor ataxia. In the latter case there is no paralysis; the muscles have preserved their force, but the movements are no longer co-ordinated. At each step the leg is thrust too far forward and outward; the movement exceeds the end and the patient brings back the leg, but brings it too far back; and the leg, being in a posture of extension, falls upon the ground with a stamp of the heel. When the eyes are closed, this *ataxic gait* is exaggerated to such a degree as to render walking impossible in certain cases. Indeed, it is in this manner that the victim sometimes recognises his condition: some day on entering a dark room he finds himself incapable of taking a step.

While the diagnosis is easy in advanced cases, it becomes a task of considerable difficulty when ataxia is slight. Various procedures are then resorted to which reveal the milder manifestations. The patient is asked to turn back abruptly or to stand upon one foot; it is then noticed that he does so with great difficulty or clumsiness.

Sclerosis of the posterior columns characterizing ataxia may coexist with sclerosis of the antero-lateral columns (Gowers). This is *combined sclerosis*, characterized by spasmodic rigidity of the extremities and a peculiar gait designated as *tabeto-spasmodic*.

The gait may also be disturbed by an inco-ordination or rather titubation recalling that of the drunken man—namely, *ebrious titubation*. The patient straggles, strays from the line he follows and again returns to it, loses his equilibrium and tries to re-establish it by holding the arms extended from the body in the manner of a balancing pole. This morbid state is observed particularly in cerebellar tumours. It may sometimes be associated with spasmodic gait, as occurs in multiple sclerosis (cerebello-spasmodic type), and at other times with ataxic movements (tabeto-cerebellar type of Friedreich's disease).

Lastly, there is a strange syndrome—viz., *astasia-abasia*—in which the patient, who has preserved his muscular power and is able to execute a great variety of motions, finds himself incapable of remaining in the standing posture or of walking in a normal manner; he can sometimes walk by assuming strange attitudes.

The motility of the superior extremities is appreciated in several ways. In cases of ataxia motor inco-ordination becomes manifest when the victim is asked, with his eyes closed, to touch some part of his body with the tip of his finger—the nose, for example. Finally, handwriting very readily shows the slightest disorders of motility, which thus become considerably magnified.

Convulsions.—The existence of *convulsions* is readily recognised, not only by the physician but even by those around the patient. This

syndrome is characterized by a series of abrupt and involuntary contractions, which at times last sufficiently long to keep the affected part in a determined position for a while (*tonic convulsions*); at other times they follow each other in rapid succession, producing a series of intermittent movements (*clonic convulsions*).

Convulsions may be general or local.

General clonic convulsions are observed especially in children; they occur at the beginning of or during infectious diseases, and are said to replace the chills experienced by adults. They sometimes come on as the result of some irritation, digestive disorders, intestinal worms, teething, foreign bodies, or simple emotion. Although regarded by many clinicians as commonplace manifestations, they are, even in children, really dependent upon nervous heredity.

The influence of heredity and innateness, and of antecedent causes that have acted upon the nervous system, likewise explains the appearance of convulsive phenomena in the adult. Convulsions may be manifested in the course of infections and intoxications, such as uræmia and puerperal eclampsia, but the nervous localization of the process is rather connected with the predisposition. The fact should not, however, be exaggerated. Whatever may have been the previous state of the nervous system, convulsions are inevitable in certain cases. This is what takes place in certain intoxications or infections which, like strychnine or tetanus, affect the medullary centres and there give rise to an extraordinary hyperexcitability.

Epilepsy, hysteria, and medullary lesions are among the number of nervous diseases which most frequently give rise to convulsions. It is, however, in cases of local or partial epilepsy that this syndrome becomes most interesting.

By *partial, symptomatic,* or *Jacksonian* epilepsy is meant a syndrome characterized by convulsive movements affecting a part or one half of the body. Convulsions of the hemiplegic type, which are analogous to those of epilepsy, involve progressively the two limbs and the face on one side, but they are not accompanied by loss of consciousness, at least at the beginning of the attack. The patient, therefore, witnesses his own paroxysm, and, unlike the epileptic, retains the memory of it.

Jacksonian epilepsy indicates a lesion in the hemisphere of the opposite side and serves diagnosis at least as a guide to localization. In fact, it will suffice to remember that convulsions begin with the part corresponding to the psycho-motor zone occupied by the lesion. Hence, if convulsions first appear in the face, the lesion must be seated in the corresponding centre—namely, in the lower part of the parietal and ascending frontal convolutions; if in the hand, then the middle

part of the same convolutions is altered; if in the foot, the lesion is located in the upper part of the ascending convolutions as well as in the corresponding part of the paracentral lobe.

Tics, Cramps, Trembling, Chorea.—Certain involuntary movements, not very different from convulsions, may be considered here.

Tics are characterized by the abrupt, involuntary, and habitual contractions of one or several muscles describing a co-ordinated movement. They are commonly observed in the muscles of the face.

In some cases tics constitute almost a morbid entity, the so-called *disease of tics*, the clinical picture of which is completed by what is known as *coprolalia* and *echolalia*. Echokinesia is also observed, which permits identification of the disease of tics with the jumpers' disease of Maine and Canada (Beard), latah of Java (O'Brien), and myriachit of Siberia (Hammond).

In general, tics are readily recognised. Paramyoclonus multiplex is distinguished by the character of the jerks, which do not, as a rule, involve the face and rarely outline a co-ordinated movement. Tics are not to be confounded either with occupation cramps, which are manifested on the occasion of certain movement, such as the cramps of writers, telegraphers, and pianists.

Trembling or *tremors* is a motor disturbance of great semeiological importance. It consists of a series of short oscillations which do not interfere with voluntary movements except by simply diminishing their precision.

Three varieties of trembling motions have been distinguished: (1) those with rapid rhythm, having from 8 to 12 oscillations per second; (2) trembling of medium rhythm, having from $5\frac{1}{2}$ to $7\frac{1}{2}$ oscillations; and (3) slow trembling, not presenting more than 4 or $5\frac{1}{2}$ per second.

Tremblings are also divisible into two types according as they are more marked at rest, disappear during voluntary movements (paralysis agitans), or begin with the movements and become more and more pronounced as the end is approached (multiple sclerosis). It is possible also to speak of general, or at least extensive, trembling and of one limited to a limb, assuming at times the hemiplegic type.

Chorea is an affection observed mostly in children, having a duration of from two to four months. This is Sydenham's chorea. When it appears in the aged it is incurable, and is known as Huntington's chorea.

Chorea should not be confounded with certain morbid states which from their causation, evolution, and even symptoms are quite distinct from it. Such, for example, are the electric chorea of Dubini, the electric chorea of Bergeron, the fibrillary chorea of Morvan, Salaam's tic, and more particularly hysterical chorea, the rhythmical, co-ordi-

nated jerks of which often represent the designed motions of the patient's occupation or trade, but are quite different from the purposeless and illogical movements of true chorea.

Hemichorea is characterized by truly choreic movements, except that these are limited to one half of the body and appear in the course of, or consecutively to, hemiplegia of cerebral origin. Moreover, the limbs attacked with hemiplegia are at times agitated by involuntary movements analogous to those of chorea, but are accomplished with extreme slowness. This is *hemiathetosis,* first described by Hammond, which is dependent upon cerebral lesions. When both sides of the body are involved the morbid state is generally congenital and often accompanied by intellectual defects, idiocy, imbecility, or epileptiform attacks. They are attributed to diffuse lesions of the brain with involvement of the posterior segment of the internal capsule.

Reflexes.—The investigation of motor disturbances must be completed by testing the state of the *reflexes.*

The *tendon reflexes* are first examined. Such is the name given to contraction suddenly produced in a muscle when its tendon of insertion is struck. The patellar tendon is the one commonly chosen for this research. The patient sits upon a table or upon the edge of his bed, with the legs hanging. Or he may be seated upon a chair and requested to cross one leg upon the other; or, if he is reclining, the lower part of his thigh is raised and supported by the examiner's left arm. The patellar tendon is then percussed either with the tips of the fingers or with the ulnar edge of the hand. Under normal conditions, a sudden contraction of the quadriceps femoris is obtained, and the foot is thrown forward. Under pathological conditions, the reflex may become increased; in certain cases it is so exaggerated that the effect, exceeding the region excited, is expressed by an abrupt movement of both lower extremities. In other instances, it is diminished or even abolished. In the latter case it is well to begin the exploration by asking the patient to strongly press the hands one against the other; in this manner all involuntary contraction in the lower limbs is suppressed and the reflex sometimes reappears.

Increase in the patellar reflex is observed in a great number of affections, particularly in all those in which contracture exists. When it appears in the course of flabby hemiplegia, it indicates that contracture is imminent.

Among those diseases which give rise to increased patellar reflex may be cited multiple sclerosis, transverse myelitis, sclerosis of the pyramidal column, lateral amyotrophic sclerosis, certain medullary compressions; intoxications, such as hydrargyrism; and neuroses, as neurasthenia. As to suppression of the reflex, it is met with in loco-

motor ataxia (Westphal's sign), pseudo-tabes from peripheral neurites, infantile paralysis, acute spinal paralysis, and certain circumscribed compressions of the cord.

When the patellar reflex is very markedly exaggerated another morbid phenomenon designated as *epileptoid trepidation* may be called forth. The patient being on his back, the ends of the toes are grasped and abruptly extended; rapid contractions are immediately produced in the triceps, which are expressed by a series of movements of extension and flexion in the foot. In some instances the same experiment elicits a spasmodic contraction that maintains the foot for a few moments fixed in the position given to it.

The tendon reflexes may also be tried in other parts of the body—for example, in the wrist or in the lower jaw—but it is of far less importance than in the knee.

More interesting are the *superficial reflexes,* and among these the cutaneous reflexes. In this connection are investigated the effects produced by tickling the sole of the foot, by exciting the muscles of the abdomen or of the anal region, and the " cremaster reflex," which is elicited by excitation of the inside of the thigh and is attended by retraction of the testicle. This reflex is especially intense in children.

The reflexes that may be produced in certain mucous membranes should next be sought for. The nauseous reflex, the nature of which is sufficiently obvious from its name, is elicited by touching the palate or the fauces; it is absent in various nervous diseases, particularly in hysteria. Excitation of the conjunctiva arouses a reflex contraction of the eyelids. Excitation of the glans penis produces contraction of the urethral bulb, known as the bulbo-cavernous reflex, etc.

Contractions appearing at times in muscles when percussed should not be mistaken for reflexes. This phenomenon, designated as *idiomuscular contraction* or *myoidème,* is obtained especially in the pectoral muscles and the biceps. By slightly tapping over the former a series of fibrillary contractions are caused, which appear as a cord beneath the skin. As to the biceps, the muscle is taken hold of between two fingers, forcibly raised and dropped, when a transverse ring becomes manifest. This phenomenon is frequently observed in wasting diseases and in cases of rapid emaciation. It is very well marked in tuberculosis and often more accentuated upon the more profoundly affected side.

SENSIBILITY.—The sensory disturbances may be divided into two groups: those of which the patient is conscious and for which he generally seeks medical advice, and those which the physician must carefully look for.

The former are subjective symptoms consisting of pains or anomalous sensations.

Pains possess a high degree of importance in semeiology.   From the beginning of the interrogation they lead the physician to the path of diagnosis, drawing his attention to a region or organ.   In fact, it is of greater consequence to determine the seat than the character of sensations experienced.   Of course, in certain cases the information given by the patient as to the sensory phenomena from which he suffers is of interest: the sharp, pulsatile, shooting, fulgurating, drawing character of the pains sometimes guides the physician.   In general, however, it is better to lay stress upon the location.   After the region is decided, it is necessary to determine whether the pain is superficial or deep seated, diffused or confined to a limited territory, in an organ or in some important part of an organ, occupying the surface of a muscle or following the course of a nerve.   When these primary results are obtained, then the region is carefully palpated to decide whether pressure increases or diminishes the pain, whether some spots are more painful than others, and whether voluntary or passive movements cause exacerbation.   Likewise, it is well to determine whether certain external conditions modify the sensations complained of.   For example, one pain may be relieved by cold, another by heat, and a third may become intensified during the night.   The nocturnal exacerbation of cephalalgia points decidedly to a syphilitic origin.

Furthermore, it should be borne in mind that the site of pain is not necessarily connected with the seat of the lesion.   When a nerve is compressed the phenomena of pain are not pronounced at its terminations.   The same is true of diseases of the spinal cord.   The gastric, the fulgurating, and the girdle pains of locomotor ataxia are peripheral manifestations of the central lesion.

Finally, when pains express some general derangement, their location is no longer of any importance.   Headache, of which patients so often complain in the course of the most varied morbid states, should not lead us to look for or admit an intracranial lesion.   Rachialgia, which is so frequent at the beginning of certain eruptive fevers—in smallpox and more rarely in measles—indicates at most a certain congestion in the spinal cord, without being of itself of any value with reference to localization.

Then the patient must be questioned whether he has experienced any anomalous sensations—formication or subjective impressions of cold or heat.   Under a great variety of circumstances, and notably in neurasthenia, the patients complain of flashes of heat; in paralysis agitans they are always too warm.   Lastly, a painful or troublesome sensation may be felt along a limb or a nerve and precede a nervous

attack, particularly an epileptic paroxysm: the phenomenon is designated as an *aura*.

After having interrogated the patient, the sensory disturbances are to be sought for, and to this end the thermal and the tactile sensibility, as well as the sensibility to pain, must successively be examined.

Tactile sensibility is tested by the touch of a finger, or a pointed metallic object, or still better with the sharp edge of a sheet of paper. Care should be taken to avoid pressure in order not to call into play the deeper sensibility.

In investigating sensibility, we must determine whether it is preserved, diminished, or increased; whether the sensation is perceived at the excited point and corresponds to the excitation and is produced in normal time.

Sensibility may be absent all over the integument, upon the mucous membranes as well as upon the skin. This condition is hardly ever realized in any morbid state other than hysteria. In the majority of cases anæsthesia is distributed in the form of disseminated plates, at times associated with plates of hyperæsthesia, or it may affect a limb, one half of the body, or the inferior extremities. In dealing with such complex cases it is well to record the various disturbances observed upon a schematic design representing the general appearance of the body.

When the patient is still capable of feeling, it must be decided whether sensation is referred by him to the point excited. To this effect the patient is directed to close his eyes, and is then asked to tell exactly in what region stimulus is applied. It is next determined whether the sensation is precise. The patient at times perceives two contacts, while there is only one; and more frequently he declares there is but one, while there are two. In order to appreciate this phenomenon, a small apparatus called *æsthesiometer* should be used. This is much like a pair of compasses with two points, one fixed and the other movable over a graduated quadrant. By means of this instrument it can readily be determined at what distance the two excitations fuse into a single sensation.

It should also be decided whether perceptions are as rapid as in a normal state. It is to be remembered that the time elapsing is proportionately longer as the point explored is farther removed from the centres, perception being most delayed in the case of the end of the foot. In certain instances delay is long enough to be readily appreciated. When it is less marked registering apparatus must be resorted to, which can not be made use of in ordinary clinics.

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Diminution or increase in the sense of touch may coexist with analogous modifications in thermal sensibility. The most interesting cases, however, are those in which the two orders of perception are differently modified. This is what occurs in syringomyelitis: tactile sensibility is normal while thermal sensibility is suppressed, so that the patient constantly burns himself without minding it. To appreciate thermal sensibility, glass tubes containing hot or cold water are applied to the skin. When more precise information is desired, a thermometer is dipped in the tube, and very exact results are thus secured in employing liquids of gradually increasing temperature.

Sensibility to pain is appreciated by pinching or pricking the skin, or by employing an interrupted electrical current. It is thus determined that analgesia and anæsthesia do not necessarily coincide. Analgesia may even coexist with spontaneous pains, as occurs in locomotor ataxia, in compressions of the cord, and in certain forms of neuritis.

Hyperalgesia, or increased sensibility to pain, may be superficial or profound. In the latter case forcible pressure is required to produce pain in subjacent organs. It is not rare to find in hysterical individuals some deep-seated hyperalgetic zones, the excitation of which gives rise to a convulsive paroxysm, or, on the contrary, arrests one just beginning. Of these so-called hysterogenic zones the most important ones are seated at the vertex, in the dorsal region of the spine, at the nipple, under the mammary gland, in the ovarian region, in the testicles, and in the patella.

All muscular action excites subjective sensations informing us of the movement accomplished—i. e., of the force displayed and the situation of our muscles. This *muscular sense* is suppressed in certain nervous diseases. The patient is unaware of the position occupied by his limbs. If, his eyes being closed, we move his lower extremities, he is unable to tell in what position they are placed. This phenomenon, which is observed in a great number of spinal or cerebral diseases, is particularly frequent in locomotor ataxia. The patient often loses the sense of power displayed; this is a commonplace disorder and occurs in all forms of paralysis, and therefore is without value. More interesting is the loss of the sense of effort which occurs in medullary paralyses involving the glottis. This phenomenon can readily be understood in view of the fact that the integrity of the glottis is indispensable for the production of effort.

ORGANS OF SENSE.—After the examination of general sensibility, the state of the special sense—that is, of the organs of sensibility—must be investigated.

It is usual to first take up the sense of vision, which is the most important from a semeiological standpoint and the most difficult of exploration.

Leaving aside what belongs to the study of ophthalmology, we shall consider only those explorations which every physician must make.

As always, the first step is to ask the patient questions with regard to phenomena of pain. These are sometimes sensations of foreign bodies, at other times photophobia and ocular and often periorbital pains.

The visual apparatus is examined to determine successively the state of the eyelids, conjunctivæ, cornea, and iris; the state of the external and internal musculature of the eye; the sensibility of the external parts; the state of the secretions; the visual acuity and the field of vision.

The eyelids are often the seat of lesions which are without gravity—i. e., blepharitis, and particularly ciliary blepharitis, eczema, hordeolum, etc. In the conjunctivæ the state of vascularization is to be examined, and in certain instances phlyctenulæ and vegetations must be sought for. Then the cornea should be examined, which may be the seat of ulcers or cicatrices, the presence of which is of great diagnostic value, and, finally, the iris, which is at times deformed or affected with pigmentary lesions.

Then passing to the examination of the musculature, care should be taken to have the patient well facing the light. The movements of the eyelids are first taken into consideration. As already stated, the condition of the orbicularis is of considerable semeiological importance. While this muscle is affected in case of peripheral facial paralysis, it is spared in central paralyses. In other instances a spasmodic semiclosure is observed. This is blepharospasm, which, when not referable to a reflex caused by photophobia or pain (foreign body, conjunctivitis, iritis), is pathognomonic of hysteria.

Finally, ptosis or drooping of the upper eyelid is connected with a limited or extensive paralysis of the third pair. It often coexists with paralyses of the oculo-motors and dilatation of the pupils.

When the ocular globe or the eyeball protrudes between the eyelids more than is natural, *exophthalmia* is said to exist. If this symptom is unilateral, it immediately suggests a tumour of the orbit, or an abscess pushing the eyeball forward. Bilateral exophthalmia, which is especially pronounced in case of exophthalmic goitre, imparts to the patient an altogether peculiar appearance of astonishment.

Examination of the ocular movements may demonstrate that both eyes do not look in the same axis. This phenomenon is due either

to a defective congenital conformation or to a local or general paralysis of one or both oculo-motors. In investigating ocular paralyses the patient is instructed te follow with his eyes an object which is being displaced successively to the right, to the left, upward and downward. Knowing the physiological rôle of the various muscles, it is easily determined in which muscle or set of muscles activity has ceased. It must next be decided which nerve is affected, and whether in its entirety or in some of its branches. Then, taking into account the accompanying manifestations, it will be possible to recognise the seat and cause of the lesion of which the paralysis is but a symptom.

There is a particular syndrome—i. e., *external ophthalmoplegia*—in which all the external muscles of the eye are paralyzed. It is generally dependent upon locomotor ataxia, cerebral syphilis, exophthalmic goitre, or bulbar paralysis.

Although ocular paralyses are unilateral in most cases, they may also be double. In the latter case quite important disorders result. The paralysis causes dissimilar, nonconjugated ocular deviations. This event, of rare occurrence, is observed especially in syphilis, ataxia, and diabetes. At other times deviation is in the same direction, both eyes looking to the same side, right or left. This conjugate deviation of the eyes is met with in upper medullary paralyses; it often makes its appearance, although in a transitory manner, at the beginning of multiple sclerosis. Finally, it may coexist with a similar deviation of the entire head, and then it is called *conjugate deviation of the head and eyes*, which is of very frequent occurrence in the course of encephalic lesions. When it coincides with hemiplegia, it obeys the following two laws, which serve to determine cerebral localizations:

1. When the lesion affects the hemispheres, the patient turns away from his paralyzed limbs, or, as is sometimes said, looks to his lesion. If an excitation takes place, the attitude changes: instead of looking to his lesion, he looks to his convulsed extremities.

2. When the lesion involves the mesocephalus, the law is reversed: The patient looks at his paralyzed limbs, and turns away from them when he becomes excited. A disorder more difficult of comprehension is what is described as *asthenopia*. Contraction of the two internal recti muscles becomes insufficient for near sight—say, for reading. Then a sense of fatigue, a visual disturbance is produced. When this syndrome is not accounted for by any lesion of the eyeball or its muscles, it is due to a nervous disease, exophthalmic goitre, hysteria, and, above all, neurasthenia.

Of the disturbances of a spasmodic character, *nystagmus* deserves mention. It is characterized by oscillatory movements of the eyeballs,

usually horizontal (horizontal n.), more rarely vertical, oblique, or even rotary. It is at times congenital. It may occur in miners (n. of occupation); but it is especially frequent in multiple sclerosis, in Friedreich's disease, cerebral tumours, and encephalitis.

Then the examination of the *internal muscles* of the visual apparatus—viz., of the iris—is taken up. The points to be noted are whether the pupils are more or less dilated than normally; whether they are regular, perfectly circular, and equal. Their contractility is also tested under two different conditions: in the light and at distances. In order to appreciate the influence of light, the eyes are closed for a few minutes and then suddenly opened, care being taken to have the patient facing the light or to place before his eyes a lighted match. The pupil, which had dilated during the palpebral closure, immediately contracts. Accommodation is examined by directing the patient to look alternately at near and far objects, when it is noticed that the pupil dilates in the former case and contracts in the latter. This examination is of very great semeiological importance. Persistence of accommodation to distance with suppression of accommodation to light is a sign which is hardly ever met with in pathological conditions other than ataxia and general paralyses. It is called the *Argyll-Robertson sign.*

Suppression of the movements of the pupil is observed in lesions of the ciliary nerves or their nuclei of origin, and in inferior radicular brachial paralysis; it then coexists with miosis.

By *internal ophthalmoplegia* is designated paralysis of the internal musculature of the eye, with mydriasis as its dominant symptom. This disorder at times coincides with external ophthalmoplegia, thus constituting total ophthalmoplegia. These various manifestations are observed in tabes dorsalis, when they are generally unilateral, and in the atrophy of the nuclei of the cranial pairs, in which they are bilateral and progressive.

Tactile sensibility of the external parts is lost in certain central lesions and in hysteria. The conjunctivæ may then be touched without causing pain or palpebral contraction. This disturbance has already been referred to in connection with sensitivo-sensorial hemianæsthesias.

Conjunctival hyperæsthesia is observed in certain neuropathic subjects, and in cases of inflammatory lesions of the profound or superficial parts of the eye; when it is intense, it produces blepharospasm.

We shall not dwell upon modifications in the secretions, the study of which belongs to the domain of pure ophthalmology. It will suffice to bear in mind that, in certain cases the lachrymal secretion

flows over the cheeks, as occurs when the excretory canal is obstructed, and in cases of peripheral facial paralysis (paralysis of Horner's muscles). The quantitative modifications of the secretion have not yet been much investigated. All that has been noted in connection with this subject is the loss of the faculty of shedding tears in certain neurasthenics, and the facility with which tears are shed by hysterical individuals. The crisis of tears following a convulsive attack may be of some importance to differentiate an hysterical from an epileptic paroxysm.

The secretions of the palpebral glands are exaggerated in inflammations of the eyelids, of which they cause the agglutination. Exudates may also be produced, either pseudo-membranous, and then generally diphtheritic, or purulent. We have repeatedly referred to purulent ophthalmia, which in the majority of cases is connected with the presence of the gonococcus.

Examination of the ocular apparatus is terminated by an inquiry into the state of vision.

The points to be looked into are as follows: Ask the patient whether he suffers from any disturbance; then examine as to his vision with both eyes and with one eye, and then determine successively whether he sees the object, whether he sees it in the different situations through which it is carried, and in its real form and contour.

The troubles experienced by the patient are of several orders. At times he notices that he does see the objects as clearly as he used to, or that his sight is becoming short. At other times he complains of double vision (diplopia), or of no longer exactly recognising forms and colours. In yet other instances, false images disturb his vision; he experiences subjective sensations which he knows well to be unreal. In this last case there may be nothing more in the field of vision than some fixed or moving black spots (*mouches volantes*). At other times the illusion is more intense and is expressed by luminous sensations designated as sparkling scotoma. The patient sees before his eyes an irregularly outlined shining spot, moving slowly, and often surrounded by sparks. This phenomenon, which occurs in paroxysms, is one of the symptoms of *ophthalmic migraine,* and is frequently met with in the beginning of grave nervous diseases, such as general paralysis. It is a subjective event, which must carefully be distinguished from analogous sensations connected with optic lesions and alterations of the eyeball. In the former case ophthalmoscopic examination demonstrates the presence of lesions at the fundus of the eye; in the latter, pressure upon the eyeball produces deformation of the scotoma.

In addition to what a patient can frequently tell with regard to his visual modifications, the physician must, as a rule, look carefully for disturbances.

Diminished *visual acuity*, or *amblyopia*, is readily recognised. It remains, however, to determine its variety; whether it is due simply to a weakening of perceptions, or is referable to scotomata—i. e., blind spots in the field of vision.

For examining the scotomata the following process is resorted to: The patient is instructed to alternately close each eye, and then to gaze with the open eye at some point, while an object is displaced; the patient must tell at what moment he ceases to see the moving object.

Scotoma is central or peripheral. If it is peripheral, the moving object becomes invisible as soon as it is a little removed from the point stared at. The field of vision is then said to be narrowed.

A central or peripheral scotoma associated with loss of pupillary reflex is a symptom of optic neuritis or tabes dorsalis. The two varieties can be distinguished by means of ophthalmoscopic examination. An amblyopia of the same order is also observed in intoxications by alcohol or tobacco. In this case, however, the scotoma is central and regular. Analogous disturbances are produced under the influence of diabetes and uræmia. Narrowing of the field of vision with preservation of the pupillary reflex is one of the sure signs of hysteria.

The field of vision may become suppressed in one half of the eye, a morbid state known as *hemiopia* or hemianopsia. It may be unilateral or bilateral, occupying the external or the internal half of the visual field—in other words, the temporal or the nasal side.

A monocular hemiopia or a heteronymous bilateral hemiopia indicate a lesion of the optic nerve. Heteronymous bilateral hemiopia, which is temporal in most cases, generally depends upon a tumour of the pituitary gland, and is an important symptom in acromegalia.

Homonymous hemiopias are divided into two groups, according as the pupillary reflex is lost or intact. In the former case there is lesion of the optic nerve; in the latter, there is cortical or subcortical cerebral lesion. The variety most frequently encountered is a right lateral hemiopia, coinciding in general with word blindness, and is connected with a lesion of the curved gyrus. In this instance the patient is blind on the right half of the field of vision: he is therefore affected with right temporal and left nasal hemiopia.

Contrary to what one might believe, diplopia is a manifestation which must often be sought for. A patient who is affected with it as a result of ocular paralysis no longer perceives it after the lapse of some time, for the reason that, through a special position of the

head, he succeeds in bringing both of his eyes to the same axis; or else he unconsciously suppresses the vision of one eye. It is possible to cause the phenomenon to reappear by asking the patient to fix his view upon an object which is then moved. The paralyzed eye will be unable to follow it in certain directions, and the image, being impressed upon nonsymmetrical parts of the retina, will appear double.

Finally, if one eye of the patient be closed, and an object be presented before the other, and be carried near and far, it will sometimes happen that the individual sees at a certain distance several objects instead of one, or the object will suddenly appear to be smaller or larger. These various phenomena, designated as diplopia, monocular polyopia, micropia, and megalopia, are observed only in hysteria.

Chromatopsia is tested by presenting to the patient papers or textures of various colours and asking him to name the tints. It is preferable to give him skeins of wool of assorted colours and ask him to separate and classify them. He is then seen to confound the most sharply distinct colours.

Two orders of disturbances are distinguished in the perception of colours. There is sometimes *achromatopsia*—namely, absence of certain perceptions—and sometimes *dyschromatopsia*—i. e., confusion of colours. This latter variety is particularly frequent in hysteria; when it coexists with narrowed field of vision, it is pathognomonic of the neurosis.

Achromatopsia is met with in hysteria, tabes dorsalis, and intoxications by alcohol and tobacco. The disappearance of the different colours does not, however, take place in the same order. In hysteria, achromatopsia begins with violet, extends to yellow, green, and, much later, to red. In the other cases the perception of red is lost first. In tabes the perception of yellow persists very long; it is still present at an advanced stage when the patient has become almost blind.

Examination of the AUDITORY APPARATUS is generally made in a summary manner in current clinics.

The patient is questioned as to the sensations he experiences. The latter are divided into three classes. In some cases there is diminution of auditory acuity; in others there is increased auditory sensibility, so that somewhat strong noises give rise to painful sensations; finally, the patient may complain of subjective sensations—tingling in the ears, anomalous phenomena, murmurs, whistling, etc.

Exploration is at first confined to a search for lesions or some discharge in the external parts. Then, having the patient face the light, and strongly drawing on the pavilion of the ear, the external meatus is looked into to discover certain alterations, and especially the presence of accumulated cerumen.

Investigation of auditory acuity is readily made by means of a watch, which is at first placed at a certain distance and is then gradually brought nearer the ear. It is well to supplement the exploration by applying the watch or, still better, a tuning fork to the vertex of the head. If, under these conditions, the affected ear should hear the sounds as well as the healthy ear, it is concluded that the central parts are intact; if not, then a labyrinthian lesion is to be admitted.

The tympanum also should be examined by auscultating the ear of the patient, either by applying one's own ear to that of the patient or by employing a stethoscope or Toynbee's tube. The patient having closed his nose and mouth, the physician perceives a slight crackling murmur when the patient swallows his saliva.

In the majority of cases these various modes of exploration must be supplemented by more exact procedures. Examination of the ear necessitates the use of some special instruments. There are two which every physician should know how to make use of: the aural speculum, which permits the study of the external auditory canal and the tympanum; and the sound of Itard, which shows the condition of the middle ear by permitting catheterism of the Eustachian tube.

TASTE and SMELL become diminished or suppressed in a great number of infectious or toxic diseases. The catarrhal state of the nasal fossæ, dryness of the mouth, and coated condition of the tongue interfere with the normal play of these various parts. In other cases subjective disorders of a truly hallucinatory character are observed, along with analogous disturbances of the eye and vision. The patient complains of perception of generally disagreeable odours, or of a bad taste in the mouth, and, quite often, these subjective sensations give rise to a particular delirium: they lead the patient to the belief that he is the object of attempts at poisoning.

In exploring these two senses care should be taken to distinguish their special from their general sensibility.

Taste is tested by placing upon the tongue sweet or bitter substances, such as sugar or quinine.

Olfaction is investigated by placing under the nose aromatic substances, such as essence of peppermint, Cologne water, asafœtida, or musk. In this connection the use of irritating substances should be avoided, such as acetic acid and ammonia, which, apart from their odorous properties, possess the power of arousing general sensibility. Their nonperception indicates paralysis of the trigeminal nerve.

The various modes of sensibility may be suppressed in one half of the body. There is then a syndrome of great importance—viz.,

sensitivo-sensorial hemianœsthesia. It consists in the suppression of cutaneous and profound sensibility, of the muscular sense, of the senses of taste, smell, and hearing, along with narrowed field of vision and diminished pharyngeal reflex, while the tendon and skin reflexes, the pupillary reflex, and the response to painful impressions are normal. This syndrome is met with under two pathological conditions—viz., hysteria and lesions of the internal capsule in the sensory crossway (*carrefour sensitif*).

CIRCULATORY, SECRETORY, AND RESPIRATORY DISTURBANCES.—The frequency of vasomotor derangements has repeatedly been alluded to, particularly in connection with the integument.

The disturbance sometimes consists in vaso-constriction, which is especially marked in the extremities, as evidenced by the " dead finger," and, in a more advanced degree, syncope of the limbs, with a possible termination in small points of sphacelus. Or there may be venous congestion, or cyanosis, as occurs in asphyxia of the extremities. Finally, a congestion through active vaso-dilatation is often produced in the course of the most varied nervous diseases. Sudden redness of the cheeks in the beginning of meningitis, and the white line which may be produced with the nail upon the skin of the abdomen, are well-known phenomenon. Trousseau used to attach great importance to this meningeal streak (*raie meningée*). At the present day it is known that this phenomenon simply indicates vasomotor paralysis, and, furthermore, that in order to be worthy of consideration it must fulfil the following two conditions: appear slowly and disappear slowly.

A vasomotor disturbance may terminate in fluxions, which occur most frequently in the cervical region and mammary glands. In hysteria this gland is sometimes so voluminous and painful that it has more than once been considered as affected with cancer and treated by operation, which was at least useless.

In a more advanced stage vasomotor disorders end in a vascular rupture. The hemorrhage taking place in the skin or on the mucous membranes is expressed by bloody tears, epistaxis, hemoptysis, or hematuria. These hemorrhages are sometimes caused by organic lesions, but are due to hysteria in most cases.

It is superfluous to enlarge upon *secretory disturbances*, which have already been referred to incidentally.

Sialorrhœa is not an event of rare occurrence; a simple hemicrania or neuralgia suffices to produce it. It is at times the premonitory phenomenon of an epileptic attack.

Diaphoresis, suppressed in neuritis, is often exaggerated in cases. of neuralgia or lesions of the medulla.

Diuresis may present similar variations. As already stated, the urine increases when excitation is slight, and decreases when it is intense.

Finally, even the visceral secretions may undergo marked changes. Crises of hypersecretion of hydrochloric acid in the stomach, gastrorrhœa, and enterorrhœa are observed in diseases of the spinal cord, such as tabes dorsalis, and in neuroses, such as hysteria. They are particularly frequent in neurasthenia, although discussion is still open as to whether the digestive symptoms depend upon the nervous affection, or the latter is a product of the bad state of the gastrointestinal functions. The latter hypothesis is more plausible. The digestive derangements render the neurosis manifest in predisposed individuals.

It is also important to remember that lesions or disturbances of the nervous system often influence the respiratory function. Lesions of the medulla oblongata may give rise to dyspnœa. Weir Mitchell has described an hysterical *tachypnœa* characterized by an extraordinary acceleration of the respiratory movements, amounting in some cases to from 40 to 100 or even 120 per minute, without the patient appearing to make any effort.

TROPHIC DISTURBANCES.—Of all the nutritional disorders occurring in nervous diseases, those bearing upon the muscular system are decidedly the most important.

Muscular atrophy is readily recognised by modifications in the appearances of the affected parts. The eminences are effaced, the bones become apparent, the regions are deformed, either as a result of atrophy or by the retraction of the antagonists, whose action is no longer counterbalanced. The result is modifications which are particularly notable in the hands (preacher's hand, monkey hand, skeleton hand), spinal deviations or curvatures of a compensating nature, destined to re-establish the equilibrium. It must be noted that atrophy of the muscles is sometimes masked by adipose tissue; the latter may be seated in the muscle itself and impart to it a volume equal or even superior to the normal: pseudo-hypertrophy is then said to exist. When fat is subcutaneous, it disguises the lesion, but it is readily proved by making a fold upon it. It is then seen that the adipose coat has considerably increased.

It will not suffice to recognise the existence of muscular atrophy, its localization and extent; its invading and progressive tendency should also be determined. An attempt must then be made to establish its place in nosology. Its interpretation is often a difficult task in view of the multiplicity of clinical types. This fact may be seen from the following summary, in which the principal cases alone are included:

1. *Circumscribed Amyotrophies of Muscular Origin.* — Myositis, rheumatism, and contusions of the muscles, especially the deltoid, give rise to local atrophies, which are in no wise extensive.

2. *Amyotrophies of Articular, Osseous, and Visceral Origin.*—The lesions of articulations, from arthritis to sprain, rapidly produce atrophy of the muscles concerned in the movement of the affected joints. As already referred to (page 181), the question is one of reflex atrophy.

Fractures of the bones produce the same results. Visceral inflammations are also included among the causes—e. g., pleurisy gives rise to atrophy of the muscles surrounding the affected side.

3. *Amyotrophies of Peripheral Nervous Origin.*—Section of the nerves, neuralgias, and neurites enter into this group. The action of these is limited, while in cases of polyneuritis, which are generally consecutive to chronic intoxication by alcohol and lead, there is atrophy of the lower extremities, with suppression of the reflexes, and a peculiar gait already described as steppage. It is the syndrome otherwise called pseudo-tabes.

4. *Amyotrophies of Spinal Origin.*—These are far more numerous, and are divisible into two groups according as they are confined to a region or assume a progressive course.

Among the former may be cited infantile paralysis, acute spinal paralysis of the adult, various diffused myelites, and alterations of the meninges, especially hypertrophic cervical pachymeningitis.

The second group includes progressive muscular atrophy, of which the type first known is Aran-Duchenne's type, starting from the thenar eminences and progressively invading almost the whole body. Allied to this type is syringomyelitis, which is readily differentiated by the study of sensibility (absence of thermal sense without anæsthesia). To the same group belong progressive muscular atrophies of the scapulo-humeral type (Vulpian), certain unsatisfactorily classed types beginning with the trunk or the lower extremities, amyotrophic lateral sclerosis, and labio-glosso-laryngeal paralysis.

5. *Myopathic Amyotrophies.*—These resemble the preceding group by their progressive course, and are distinguished from them by the absence of spinal lesions. Myopathic amyotrophies include the following types: Duchenne's pseudo-hypertrophic paralysis with two subvarieties, the femoro-tibial type of Leyden-Möbius and the scapulo-humeral type of Erb; progressive myopathies, including the facio-scapulo-humeral type of Landouzy-Déjérine, the scapulo-humeral type of Immermann and Zimmerlein, and the femoro-tibial type of Eichhorst, Charcot, and Marie.

Exploration of trophic disturbances should be completed by exam-

ining the other parts of the body: the bones, which are sometimes affected, and more particularly the skin with its annexa—nails and hair.

The main disturbances have already been referred to—i. e., erythemata and vesicles of the skin, often following the course of a nerve and grouped as in herpes; also bullæ, pustules, cutaneous sclerosis, pigmentary or vasomotor disorders, eschars, and ulcerations, such as the perforating ulcer (*mal perforant*). Œdemas and pseudo-lipomata have already been mentioned. Arthropathies, which are so frequent in locomotor ataxia, deserve special mention.

INTELLECTUAL DISTURBANCES.—Abeyance of all the intellectual functions is designated as *coma*. When it comes on suddenly, it is termed apoplexy. In both cases loss of consciousness may be complete or incomplete. In the latter instance peripheral excitations elicit a vague perception; certain impressions may for a moment bring the patient out of his torpidity.

These two morbid states are readily recognised, but to determine their causation is not infrequently a task of difficulty. Etiological diagnosis can only be arrived at by taking into account the concomitant phenomena, and especially the previous disorders which alone offer precise information regarding the diseases of which these two syndromes are but epilogues.

Passing over the extreme occurrences, we shall consider the less profound disturbances that may be observed.

Sleep is modified in a great number of diseases. The patient must, therefore, always be interrogated with reference to sleep.

Infections are often from the start attended by insomnia. When the patient falls asleep he has dreams and troublesome nightmares. The same occur in the course of chronic states, especially in cerebral affections, neuroses, and intoxications, notably alcoholism, auto-intoxications, and asphyxia of individuals suffering from cardiopathies.

In children sleep is often troubled with terrible dreams, especially those who are predisposed by nervous inheritance, or who suffer from gastrointestinal disorders; in the latter case the manifestations are of the character of auto-intoxication.

Sleep, which is nearly always unsatisfactory in neurasthenic patients, may be altogether suppressed in the beginning or course of mental diseases.

Disturbances of sleep consist in sudden jerks, which awaken the sleeper, and are especially frequent in alcoholism, in the form of dreams and nightmares. Dreams of occupation are equally the lot of alcoholic subjects. A dream often has its starting point in some morbid sensation or pain. Individuals who suffer from disease of an

organ often see animals compressing or tearing the diseased parts; the results are very distressing impressions and choking. In the beginning of mental diseases nightmares are frequent, and recur night after night with identical characters, and may become the starting point of delirious conceptions, if they do not already represent a sort of unconscious delirium.

Tendency to sleep is increased under a great number of circumstances. In the course of infections the insomnia of the first days yields later on to somnolency. Finally, in many diseases, convalescence is announced by a return of a calm and peaceful sleep contrasting with the somnolency of the preceding days.

Excessive sleep may be sufficiently marked to characterize certain morbid states. Such is sleeping sickness, predominant upon the western shore of Africa, of which a slight form is observed in Switzerland, and described as *paralyzing vertigo* or *nona*. Dr. Briquet, of Armentières, published a very curious observation which seems to establish a certain relationship between sleeping sickness and myxœdema.

An irresistible tendency to sleep is observed in various patients and constitutes a symptom termed *narcolepsy*. It is of very frequent occurrence in dyspeptic and cardiac patients. When it appears, particularly after meals, it must always lead to examination of the urine, for the reason that it is often the first sign of diabetes.

Finally, hysterical patients sometimes have paroxysms of sleep, in which some authorities include the syndrome known as hysterical apoplexy. It is by the study of concomitant manifestations that a differential diagnosis can be arrived at.

Sleep may also be artificially induced, either by medicinal substances called narcotics (opium, chloral hydrate, sulphonal, etc.) or by various mechanical or physical means. Intense light, a brilliant object, a sudden noise, movements repeated before the eyes, and, with some individuals, a simple touch, induce a sleep designated since the time of Braid as hypnotic sleep.

Two varieties of hypnotism have been distinguished: a minor form, which includes various degrees from light sleep to profound sleep, at times accompanied by somnambulism, and a major form, occurring only in hysteria.

The major form of hypnotism has three stages: the lethargic, the cataleptic, and the somnambulistic stage.

In the lethargic state the subject has the appearance of a sleeper, but what characterizes this stage is the markedly increased excitability in the nerves and muscles; hence, an excitation, a light pressure upon a muscle or a nerve is sufficient to arouse a contracture far outlasting the excitation.

In the cataleptic state the subject is motionless, but his limbs retain all the positions artificially given them.

In the somnambulistic stage the patient obeys all suggestions.

Apart from these cases, somnambulism is also observed under various conditions. It is characterized by the continuation, during sleep, of the activity started during wakefulness, which is carried on in an automatic manner. This, for example, is the case with a child that gets up and walks with astonishing assurance in the most perilous places, such as the sill of a window or the roof of a house.

Akin to somnambulism is ambulatory automatism. An individual departs from home, and a few days later he finds himself in a city far away, without being able to understand how he came there.

In all these instances there is double personality: the individual forgets in one of the two states what he has done in the other; there is a double life.

Vertigo.—Of the intellectual disturbances, one of the most interesting is represented by *vertigo*. It is a subjective phenomenon, a sense of instability in space with reference to surrounding objects.

This sensation often disappears when the eyes are closed, but not always; at times closure of the eyes aggravates the trouble.

In order to form an idea of the characters of vertigo the physician is compelled to depend upon the description given by the patient. If, however, an attack be witnessed, certain bodily disturbances are observed, evidencing the suffering caused by vertigo. The face is generally pale and expresses anguish; the skin is covered with cold sweat. If the victim attempts to walk, he staggers, loses his balance, and falls; at times he can not help going on in vertiginous movements until some obstacle arrests him.

Vertigo is a phenomenon of frequent occurrence. As a transitory event, it occurs in the beginning of infectious diseases, in acute intoxications, and particularly in inebriation; it may be brought on by mechanical agents: Seasickness and swinging are familiar exciting causes. However, individual predisposition must also be admitted, since everybody does not experience giddiness under the conditions named.

Vertigo is also met with in the course of organic affections, especially in gastric derangements, and in arteriosclerosis, of which it often represents an early symptom; it is very frequent in nervous diseases, such as tabes dorsalis, multiple sclerosis, exophthalmic goitre, and neurasthenia. Moreover, it may assume a character sufficiently marked to characterize a special morbid state—i. e., Ménière's vertigo.

Psychical State.—Continuing the examination of the nervous system, certain derangements must be studied the appreciation of which is often a matter of difficulty.

It is important for the physician to be informed of the patient's character and the modifications which it may have undergone. In the beginning of most diseases directly or indirectly involving the cerebral functions, changes are observed in the affections. In some cases there is excessive tenderness, in others indifference. At times the patient is subject to paroxysms of exhilaration or of melancholy without any motive, or else he falls into a state of apathy or hypochondriasis. In yet other instances the people around the patient notice a change in his temper, which becomes strange and fantastical; he has " fits " of anger which he did not have before. As an illustration, we may cite the example of a child that, in the beginning of tubercular meningitis, and before all other manifestations, presents psychical changes which sometimes lead the physician to predict the imminence of morbid phenomena.

Psychic modifications may also affect the moral qualities, as evidenced by a tendency to mendacity, loss of moral sense, and sexual perversions. Actions considered as criminal are at times nothing more than the first manifestations of mental derangements; their real character is recognised only after the mental disease becomes clearly manifest.

At the onset of certain mental diseases, and more particularly of general paralysis, the subject exhibits an extraordinary activity well in contrast with his previous quietude. Interpretation is very delicate when a man is seen to conceive schemes and execute them skilfully, or to throw himself into an enterprise often with success in the beginning, or produce at times very remarkable works. Soon, however, defective points appear, which gradually increase and no longer leave the slightest doubt in the mind of an attentive observer as to the nature of the phenomena.

A great number of persons present derangements which are mostly stigmata of degeneration, and which consequently deserve the close attention of the physician. They are divisible into two groups: impulsions and phobias.

Impulsions bring certain individuals to the performance of acts which may simply be strange, or may border on insanity. For example, they can not help counting their steps in walking, or counting the windows on the streets which they pass through; others repeat the acts they see (echokinesia) or the words they hear (echolalia); yet others are at times compelled to utter coarse words obviously unsuitable to their education or habits (coprolalia).

By the term *phobias* are designated certain mental disturbances, as expressed by unjustifiable and at times childish fears. The dread is so intense that it prevents the sufferer from passing through a public square (agoraphobia), or from remaining in a closed room (cleithrophobia), or from touching certain objects. Similar to these phobias is the insane disposition of doubting, which is sometimes sufficiently powerful to prevent an otherwise sane individual from practising certain professions. The case of a physician is sometimes cited who had to give up his art because of a constant dread of making a mistake in his prescriptions.

Delirium.—An individual is in *delirium* when his sensations do not correspond to external objects; when his ideas do not correspond to his sensations; when his judgment and determination do not correspond to his ideas, or when his ideas, judgment, and determination are independent of his will (Esquriol).

Following Ball and Ritti, delirium may be divided into lunatic and nonlunatic.

Nonlunatic delirium is observed in infections, intoxications, and certain cerebral diseases.

In its mild forms delirium is simply dreaming in a state of half sleep. In a little more advanced stage the patient has hallucinations; he often attempts to rise, to run away, either to escape from imaginary enemies or to respond to calls he believes he hears, or to advance toward objects he believes he sees. In its most violent forms, delirium is expressed by incessant agitation, cries, and misdirected movements.

Without dwelling upon these varieties or their causes, it will suffice to cite as examples the generally calm delirium of typhoid patients; the noisy agitation of alcoholics (delirium tremens), which is so often occasioned by pneumonia, the noisy and tumultuous delirium observed in cerebral rheumatism; the delirium of convalescents, of starvation, of cardiac and tubercular patients, and the delirium of puerperal women, which is frequently connected with albuminuria. The organic lesions, especially those of the liver and kidneys, play an important rôle in the causation of delirium by favouring auto-intoxication of the organism.

Lunatic delirium may be total or partial. When total, it is characterized by disorder of all the psychic faculties. Of this, two clinical forms have been recognised: the *maniacal* form, remarkable for the exaltation, and the *melancholic* form, marked by persistent depression of spirits. When these two forms follow each other, then *circular* insanity is said to be present. Finally, under the name of *mental confusion* have been described cases

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in which all ideas are confounded and dissociated; speech is incoherent and all sensations and perceptions are defective or inexact.

Partial lunatic delirium consists in disturbance of one or of several psychical functions. It may affect the sensations, the thoughts, the sentiments or action.

Delirium of the senses includes illusions and hallucinations.

Illusion is belief in an image not corresponding to the sensation perceived.

Hallucination is that state of the mind in which the conceived image does not correspond to any sensation.

In the former case the object exists and sensation is real; in the latter, both object and sensation are absent. Thus, for example, a patient sees a dog and takes it for a fantastic animal. This is illusion. He hears the throbbing of his arteries and believes that he hears the discharges of electrical machines: this, too, is an illusion. These two illustrations give an idea of the two varieties of illusions that can be admitted: One originates from an external impression; the other from an internal sensation.

There are hallucinations of the senses and general or special sensibility, particularly the genetic sensibility, without the existence of any external or internal excitation to account for their development.

The deliriums of intelligence are extremely varied and may be divided into eight groups (Ball and Ritti). They are (1) ideas of satisfaction, greatness, and fortune; (2) religious ideas; (3) erotic ideas; (4) ideas of persecution; (5) ideas of humility and despair; (6) hypochondriacal ideas; (7) ideas of corporeal transformations, which consist in the patient's belief that he has changed his sex or has been transformed into an animal or vegetable; (8) delirious ideas with conscience, including insanity of doubting, hypochondriasis, phobias, and impulsions.

Impulsion leads to insanity of action. In contradistinction to this form should be placed those cases in which all action becomes impossible, either because the patient no longer has the desire or the strength to act, or because he is dependent upon some external power which arrests him.

Finally, there is also *dementia*, which consists in the loss of the mental faculties. This state is always an acquired one, while *idiocy* is always congenital.

Troubles of Speech.—The disorders in making use of signs, whether for expressing or for understanding the ideas and feelings, are called disorders of speech or language.

Blocq and Onanoff, from whom we borrow the definition above given, divide the disturbances of speech, or asymbolia, as follows:

FORMS.... Apraxia.

GESTURES. Amimia..... { Receptive. / Motor.

SOUNDS...
- Lalopathy ..
  - Dysphonia............. { Dyslalia. / Dysarthria.
  - Dysphasia (Aphasia).
    - Receptive. { Word blindness. / Alexia.
    - Motor .... { Aphemia. / Agraphia.
- Amusia ....
  - Receptive. { Sensory amusia. / Musical alexia.
  - Motor .... { True motor amimia. / Musical amimia. / Musical agraphia.

Notwithstanding their considerable number and complex appearance, these various forms of asymbolia are easily kept in memory and readily recognised.

Apraxia is a disturbance of appreciation of geometric forms. The patient does not recognise the objects he sees and makes use of them for purposes for which they are not intended. For example, he takes a plate for a saucepan and places it upon the fire.

Amimia means forgetting the sense attributed to gestures. At times the patient can not understand the gestures performed by others: this is receptive amimia; at other times he is unable to perform them correctly: this is motor amimia; he will shake his head from right to left to say yes, and from above downward to say no.

The disorders of phonetic language are more important. They are called *lalopathy* when they bear upon the speech. Lalopathy may result from some difficulty in the formation of sounds (dysphasia), either by reason of a lesion in the phonal apparatus, tongue, lips, or larynx (dyslalia), or by reason of nerve lesions preventing the regular play of the same parts (dysarthria), as occurs in general paralysis and multiple sclerosis.

Aphasia can no longer be defined to be the loss of articulate speech. It is absolutely necessary to introduce a fundamental division into its study. In fact, there is a receptive or sensory aphasia, in which the patient does not understand one of the forms of articulate language. When he has become incapable of apprehending the sense of words, although his auditory apparatus is intact, he is said to suffer from *word deafness*. When he is incapable of reading with an intact visual apparatus, he is said to be affected with *alexia*. The latter is divided into two varieties: *letter blindness*, in which the

patient no longer recognises the letters, and *word blindness*, in which he no longer understands what word is represented by the association of the letters.

In motor aphasia the victim is no longer able to employ the conventional signs of language. At times he loses the use of the signs of speech (spoken language), this being *aphemia*, or aphasia properly so called; at other times he is incapable of expressing his thoughts by writing: this is *agraphia*.

Finally, introducing into the study of the musical faculty divisions analogous to those admitted for language, a *receptive* or sensory *amusia* and a *motor amusia* have been described. Sensory amusia includes the true sensory amusia in which the patient no longer distinguishes sounds, and *musical alexia*, characterized by inability to read the notes. Motor amusia comprises motor amusia, properly so called, when the patient can not sing; musical amimia, when he can not play upon an instrument, and musical agraphia, when he can not write the notes.

We can not dwell upon the numerous clinical forms observed, which result either from association of various manifestations or from the variable intensity of the disturbances.

When the question is one of aphasia, it is easy, after having determined the variety, to recognise the part of the brain affected. It will be remembered that the seat of aphemia is in the third cerebral convolution; word blindness is localized in the angular and inferior parietal gyri on the left side, word deafness in the middle part of the first temporal convolution, agraphia at the foot of the second frontal. This last localization is the least certain.

It is also possible to determine whether the lesion is seated at or beneath the cortex. To this effect the patient is asked to indicate upon his fingers the number of syllables contained in each of the words which he can not pronounce. If he succeeds, the lesion is subcortical. This is *Lichtheim's sign*, the value of which, however, is still in dispute.

Finally, the cause of aphasia is to be investigated.

Aphasia is divided, according to its course, into transitory and permanent.

Transitory aphasia is observed in auto-intoxications, diabetes, albuminuria, gout, dilatation of the stomach, and, in children, in the course of a simple indigestion. It occurs in some infections, as, for example, typhoid fever and malaria. It is often met with in nervous diseases. It may at times be caused by anger or emotion. It is especially frequent, however, in ophthalmic hemicrania, hysteria, epilepsy, general paralysis, and tumours, and, above all, in syphilis of the brain.

Permanent aphasia is produced by a destructive lesion. It depends upon cerebral softening, sometimes upon hemorrhage; it is often encountered in case of tumours, syphilis, and acute or chronic meningitis.

The preceding study of nervous disturbances demonstrates that they may occur in the course of the most varied diseases. On the other hand, nervous affections may influence all the other functions. It will suffice to recall urinary and genital disorders, the so-called nervous dyspnœa, cardiac palpitations, false angina pectoris, secretory derangements, hemorrhages, hysterical tympanites, trophic disturbances, and, lastly, the fever which, in a great number of cases, is due simply to irritation of the nervous system.

CHAPTER XXII

CLINICAL APPLICATION OF SCIENTIFIC PROCEDURES

Physical procedures—Mensuration—Examination of deep-seated parts—Cathodic
rays—Spectroscopy—Thermometry—Exploration of the neuromuscular sys-
tem—Registering apparatus—Chemical procedures—Clinical examination of
the urine, secretions, and blood—Microscopical examination—Examination of
the urine, sputa, and blood—Bacteriological examination—Direct examination
—Cultivation—Serum diagnosis—Animal inoculation—Exploratory punctures
and incisions.

EXAMINATION of the sick by means of the simple procedures thus
far indicated suffices to establish diagnosis in the majority of cases.
Therefore, when the questioning of the patient is completed, and his
personal and hereditary antecedents have been noted, when his sub-
jective disturbances have been considered, and all his organs and
tissues systematically examined by means of inspection, palpation,
percussion, and auscultation, and when the characters of his secre-
tions and dejecta, urine, vomited and fæcal matters have been ob-
served, a conclusion should be arrived at.

It is often useful, however, and at times necessary to supplement
examination by means of more precise and delicate procedures. The
latter are very numerous. We shall indicate the principal ones—i. e.,
those which are of real service—among which some, as for example
thermometry and chemical analysis of the urine, are indispensable.

PHYSICAL PROCEDURES.—The physical procedures most frequently
made use of clinically respond to three indications: (1) They aid
the usual modes of exploration; (2) they serve for the exploration
of the inaccessible or hardly accessible parts of the organism; and (3)
they furnish a precise measure of certain acts and phenomena.

In connection with certain organs, and particularly in reference
to circulation and respiration, we have shown how they can be ex-
plored by means of four simple methods—viz., inspection, palpation,
percussion, and auscultation.

Inspection and palpation furnish information as to the form and
size of regions. For greater accuracy the homologous parts are meas-

ured by means of a ribbon or string. In order to appreciate atrophy of a limb, its circumference is measured and compared with that of the healthy side. Care should, however, be taken to apply the ribbon to exactly the same region. In the case of the thorax, half of the circumference is measured from the spine to the border of the sternum, while deviations are appreciated by means of a string stretched from the notch of the sternum to the middle of the pubis (page 431).

Various apparatus have been invented for the more precise accomplishment of these examinations. Voillez proposed measurement of the thorax by means of a metallic tape formed of articulated links, called a *cyrtometer*. For mensuration of the thoracic and abdominal regions the *calipers of thickness* are mostly employed. Baudeloque's calipers, which are in general use, consist of two branches measuring about 20 centimetres in height. Each branch is made up of a straight portion, which is near the joint, and a curvilinear portion. At the point of junction a graduated quadrant is found upon which the distance between the two terminal parts can be read in centimetres.

To-day no apparatus is any longer made use of in percussion. Auenbrugger, who endowed science with this important mode of exploration, practised immediate percussion. With the fingers of the hand he tapped directly upon the part to be examined. This procedure has given way to mediate percussion, which is practised in three manners: (1) By striking with the fingers of the right hand upon one of the fingers of the left hand applied over the part; (2) by striking with the fingers upon a small plate (Piorry's *pleximeter*) of metal or ivory, and (3) by striking upon the locality by means of a hammer.

The pleximeter, which is still in use in foreign countries, has been almost entirely abandoned in France. Peter's *plexigraph*, which consisted of a cylinder upon which percussion was made and which carried a dermographic pencil at its lower part, has also become obsolete. Only the dermographic pencil (a pencil with aniline violet) is frequently used to trace upon the skin lines indicating the limits of the organs and the areas of flat zones.

Blanchi has of late presented to the profession a very ingenious apparatus, the *phonendoscope*, which enables one to very exactly outline the principal viscera.

Auscultation, as well as percussion, is generally made without any apparatus. The various stethoscopes, however, are still quite frequently employed. Though useless for the study of the respiratory organs, they serve in locating cardiac murmurs and determining their propagation. They are indispensable in the exploration of regions where the ear can not be well applied. Auscultation of cervical blood

vessels, of the femoral artery and abdominal aorta could hardly be accomplished without a stethoscope.

This instrument also serves for the auscultation of the larynx or esophagus at the cervical region. It is also employed in auscultating the ear. In the case of the organ last mentioned, however, Toynbee's otoscope is commonly made use of. It is a simple rubber tube, 70 or 80 centimetres long, the ends of which are tipped with ivory; one end is inserted into the ear of the patient, the other is applied to the ear of the physician. The patient is then asked to swallow saliva, having the nose and mouth closed, when a crackling murmur, produced by the tympanum, is heard.

It was at one time believed that excellent results would be obtained by applying for auscultatory purposes apparatus capable of re-enforcing sound. The microphones employed to this end have not, however, afforded any advantages.

Exploration of Deep-seated Parts.—One of the simplest instruments for the exploration of deeper parts is the *tongue depressor*, which may be replaced by a spoon, permitting examination of the pharynx, tonsils, and base of the tongue as far as the epiglottis.

With the same object in view, *speculums* are used which render possible inspection of canals naturally closed. These instruments are cylindrical or conical tubes which are introduced into the canals, or apparatus with valves are introduced closed, and when opened they dilate the parts to be examined.

For examination of the vagina and cervix uteri either cylindrical specula, with or without solid cylinders, which facilitate introduction and are drawn out when the instrument is in its place (Récamier's, Dupuytren's, Mademoiselle Boivin's, and Fergusson's speculums), or specula with valves are made use of. Of the latter, the one most commonly employed is the bivalve speculum of Cusco. It is also possible to explore the organs by means of a single valve (Sims's speculum).

These apparatus bring to view the state of the vagina (for this canal Sims's speculum is alone available), and especially the condition of the cervix uteri.

Analogous specula are used for exploration of the rectum, nose, and ear.

For the nasal fossæ a small bivalve speculum is generally employed; for the ear, a small tube with an enlarged end. If the organ to be explored is more deeply seated, or if it is situated at the end of a sinuous canal, recourse is had to apparatus which bring it into view by reflected light or by transparency. In the first case, mirrors are made use of. The luminous rays coming from without are sent toward the organ, and the intensely lighted image becomes visible upon the

mirror.   According to this very simple principle are constructed the *laryngoscope*, which, when introduced into the fundus of the throat, permits exploration of the larynx; the *rhinoscope*, which brings to view the posterior orifice of the nasal passages; the *ophthalmoscope*, which shows the fundus of the eye, and the *endoscope*, which enables parts hidden behind a narrow canal, and especially the bladder, to be appreciated.

When the canals are too long or too sinuous to allow the use of mirrors, the cavities are lighted and seen by transparency through the walls.   To this end small electric lamps are used which are lighted after introduction into the organ to be examined.   This method has been resorted to especially for exploration of the stomach.

There are a great number of instruments which, through the tactile sensations they produce, furnish information as to the state of various organic canals or passages.   Their use constitutes a method called *catheterism*, consisting in the introduction of rigid or flexible sounds, and in the appreciation of the state of the parts from the resistance experienced in performing the exploration.   In this manner the urethra, ureter, uterine cavity (hysterometer), rectum, esophagus, and the lachrymal canal may be catheterized.   A sound may also be introduced into the Eustachian tube; in this case, however, the end of the instrument alone is engaged in the orifice of the tube; the exploration must be completed by insufflation of air, which immediately escapes through the external ear if the drum is perforated. To this end air may also be injected into the nasal cavities by means of a rubber pump, while the patient swallows saliva, having the nose and mouth closed.   This is what is known as Politzer's procedure.

Catheterism is also employed for the examination of pathological canals.   Stylets and sounds, when introduced into fistulæ, reveal their state, length, direction, and termination.

Finally, catheterism of the internal organs has also been practised in some instances.   After a laparotomy a sound has been introduced into the biliary passages.

Of late, since Roentgen's discovery, a new method has been invented.   The human body has been explored by passing through it *cathodic rays* and by utilizing either photographic proofs or fluoroscopy.

This procedure renders considerable service in the detection of foreign bodies; it not only permits discovery of their presence, but it enables recognition of their exact situation and greatly facilitates surgical intervention.   This mode of exploration is also available in the case of concretions formed within the organism, especially for the investigation of vesical calculi.   Moreover, it renders service in osseous

and articular affections, and in fractures and traumatic dislocations. It is of less importance in internal pathology; it has, nevertheless, revealed the presence of aneurisms and furnished data in reference to pleural exudations, and particularly with regard to the state of the lungs when incipient tuberculosis is suspected.

The use of spectroscopy is one of the most interesting applications of light to clinical purposes. Hénocque has well pointed out the great benefit to be derived from this mode of exploration. He has directed the construction of an apparatus which can be applied to the surface of the thumb and permits the study upon the living subject of the rapidity of the reduction of hemoglobin. It suffices to place a ligature at the base of the phalanx; under normal conditions, at the end of from thirty to a hundred seconds, the hemoglobin is reduced, and the two dark absorption bands given by it in the spectrum disappear.

Weighing.—Another method derived from physical sciences is utilization of the various procedures of mensuration of phenomena.

In the first place, among simple procedures the *balance* may be mentioned. It is impossible to exaggerate the advantage which can be obtained by causing the patients to be frequently weighed. In the course of chronic diseases, especially in pulmonary tuberculosis, variations in the weight furnish important data, and oftener and better than any other procedure enable one to judge whether the pathological process is improving or being aggravated.

With the newborn weighing is indispensable. The infant must be weighed in order to determine whether it is growing. During the first months growth should amount to 20 or 25 grammes daily. If the child gains less than this, it is due to defective alimentation, or to the fact that the nurse is not a good one, or the feedings are not separated by well-advised and regular intervals, or the amount of milk ingested is too great or too small. In such instances the infant should be weighed before and after each nursing; the increase in weight should amount to 80 or 100 grammes.

Thermometry and Calorimetry.—Another proceeding as simple and important as the preceding one is the study of *temperature.*

In studying organic heat, four points may be taken into consideration: peripheral temperature, central temperature, temperature of certain organs or regions, and the heat dissipated.

Temperature is determined by means of small thermometers graduated generally between 30° and 45° C., or 95° to 110° F. Except in certain rare cases, central and peripheral temperatures follow a parallel course. Exploration of one of them is commonly regarded sufficient. When peripheral temperature is looked for, the thermom-

eter is placed in the axilla or in the groin, while for central temperature it may be put in the mouth or beneath the tongue; in the latter case, however, the evaporation produced by the breathed air interferes with the results. It is preferable to introduce the instrument into the rectum or vagina. In children, rectal temperature should always be taken.

In febrile diseases the temperature is usually taken morning and evening. In the majority of instances two daily explorations are sufficient. In case of grave fevers, however, thermometry must be practised at shorter intervals. In the hospital of Porte d'Aubervilliers, which is devoted to infectious diseases, the temperature is taken every three hours, and from this is derived guidance for the treatment with cold baths.

It will not suffice to learn each day the state of temperature; the daily variations must be compared. The course of the febrile movement is of the highest importance for diagnostic and prognostic purposes. It is therefore necessary to record the temperatures each day. To facilitate this task, the graphic method is resorted to quadrilaterally. Ruled charts are used, the vertical lines corresponding to days and the horizontal lines to thermal degrees. In recording the figures upon the chart a curve is designed, a glance at which permits recognition of the daily modifications in the febrile process. The various types have already been referred to in connection with the evolution of infectious diseases (page 369).

Local thermometry furnishes indications of particular interest from the standpoint of pathological physiology, but it has not entered into everyday practice. The same is true of *calorimetry*. It would, of course, be interesting to know the quantity of heat emitted by a patient, but the apparatus are cumbersome and expensive; they often give information lacking in precision, and are not yet available for ordinary clinical purposes.

Exploration of the Neuromuscular System.—A great variety of apparatus has been invented for mensuration of various functions. The apparatus are divided into two groups: some are simply instruments of exploration, others record graphically the activity of the parts.

In the first place, general sensibility and the organs of sense may be investigated.

Examination of sensibility is satisfactorily made without the assistance of apparatus. There exist, however, serviceable instruments, such, for example, as the *æsthesiometrical needle* of Beaunis, consisting of a needle supporting a plate which is charged with weights. Weber's *æsthesiometer,* which is more commonly used, is essentially composed

of two hands, of which one is fixed and the other movable upon a graduated quadrant. It serves to determine at what distance two impressions become distinct or fuse—i. e., give two sensations or a single one. Liégeois has invented an analogous apparatus for the appreciation of thermal sensibility. The two points are connected with two reservoirs, which are filled with liquids of different temperatures.

A certain number of instruments are also employed for examination of the organs of sense. There are olfactometers for testing the smell, which are useful in physiology, but too complicated to be utilized in medical practice.

For testing the taste, sapid substances are placed upon the tongue; a faradic current is at times resorted to, which normally gives rise to an acid sensation. For testing the hearing, a tuning fork is generally made use of. For the visual apparatus recourse is had to very different procedures, according to the particular exploration required.

Visual acuity is appreciated by means of charts with printed characters of various sizes. For the study of colours, disks or papers of various colours are used. Finally, although the field of vision may be appreciated by the simple procedures already described (page 477), a special apparatus, the *campimeter*, is often made use of for greater precision. It is a moving circle; the patient takes his position in the centre, gazes at a point, and indicates when he perceives and when he ceases to see a small white paper carried upon the circle. The division to which the limit of perception corresponds is then noted.

In exploration of muscular contractility the points to be appreciated are whether the power is preserved and whether the muscle contracts in a normal manner.

Muscular power is tested by means of the *dynamometer*. The individual exerts pressure upon a metallic ellipse bearing at its centre a needle which records the number of kilogrammes equivalent to the contraction.

The investigation of contractility requires the use of *electric currents*. Both continuous and interrupted currents should be successively applied to the muscles and nerves.

It is well to determine beforehand the resistance of the body to the passage of the current; this is readily established by noting the number of millimetres deviation of the needle of the galvanometer for a given galvanomotor force.

For exploration of muscles the larger electrode is placed upon the sternum or the spine; the other, the so-called *labile electrode*, is carried around upon the various parts. It must first be determined

whether the muscular contractions produced by a given current are equal to, less, or greater than those observed in a physiological state. This point may readily be determined by comparison with a healthy subject or with those muscles of the patient which have remained intact.

The qualitative modifications should next be investigated. It is to be borne in mind that, under normal conditions, effects vary with the pole considered. A weak current produces a contraction of *closure* at the negative pole. If the intensity increases, the positive pole causes a contraction which, although milder, outlasts closure as well as opening. Finally, a very strong current causes a contraction of opening at the negative pole, but at the moment of closure a real tetanization occurs. These various results are expressed by the following formula: *

$$\text{KaSTe} > \frac{\text{AnOZ}}{\text{AnSZ}} > \text{KaOZ}$$

In a great number of neuromuscular alterations the formula is reversed. *Reaction of degeneration* (Rd) is then said to exist:

$$\text{AnSZ} > \frac{\text{KaSZ}}{\text{KaOZ}} > \text{AnOZ}$$

In grave cases galvanic contractility disappears: AnSZ is the last persisting reaction.

While these changes in galvanic contractility are produced, faradic contractility of the nerve or muscle diminishes or even disappears. In order for Rd to be complete the two orders of modifications must coexist.

Sensitiveness to faradic currents is diminished in atrophies and suppressed in neurites, acute diffuse myelitis, and infantile paralysis; it is increased in certain affections, such as tetany. In Thomsen's disease the mildest faradic stimulation of the muscles gives rise to contracture.

Mensuration of Cavities.—It is useless to dwell upon the various instruments designed for the measurement of the *capacity* of apparatus and reservoirs. Recourse is at times had to *spirometers* to appreciate the respiratory capacity of the lungs. To this end, the apparatus of Hutchinson and Wintrich, or that of Boudin are made use of. The former essentially consists of a bell plunged into a reservoir full of water and kept in equilibrium by a counter weight. The patient

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* The meaning of the letters is as follows: Ka, Cathode or negative pole; An, anode or positive pole; S, Schliessung or closure; O, Oeffnung, opening or rupture of the current; Z, contraction; Te, tetanic.

executes inspiratory and expiratory movements through a rubber tube into the bell, the displacements of which, under the influence of the changes in pressure, are indicated by a moving index. Boudin's apparatus consists of a rubber bulb into which the patient expires: the bulb swells in proportion to the volume of air sent into it, and its amplification is appreciated by means of a graduated lever which it raises.

Finally, the subject may also be instructed to breathe into a *manometrical* tube or *pneumomanometer*; the oscillations of the mercury indicate the force of respiratory pressure.

Registering Apparatus.—The recording apparatus employed in clinical examination are very numerous. They are constructed so as to trace upon a moving paper the movements produced in different parts of the organism. According to the organ explored, the inscription is made either directly by means of a lever displaced by the moving organ, or indirectly by aerial transmission. In the latter case, the moving organ compresses or distends an elastic bulb communicating with another bulb provided with a registering stylet; the inscription is made upon a more or less rapidly moving cylinder.

The graphic method has been applied especially to the study of muscular contractility, movements of the thorax, and the cardio-vascular apparatus.

The muscles may be examined as to their power and manner of contraction.

There are registering dynamometers or *dynamographs* in which muscular effort is expressed by the tracing of a line. The apparatus most interesting from this standpoint is the *ergograph*. Suppose the upper limb is to be explored. It is attached to a table, the anterior surface directed upward. The hand or, still better, a single finger is left free, to which is fixed a ring provided with a thread passing over a pulley and attached to a plate charged with weights. The patient is instructed to regularly execute movements of flexion and extension; the weights, constantly raised and lowered, impart to the pulley successive rotations in reverse directions; the pulley, being provided with a stylet which records the movement upon a cylinder, gives a tracing, which becomes more and more irregular as fatigue increases.

By means of similar procedures—for example, by uniting the segments of a limb with exploring drums—it is possible to study the mode of muscular contraction either under the influence of will or of excitants, especially of electrical stimulation.

It is often useful to record anomalous movements—e. g., the contractions of tics, paramyoclonus, and tremors. In the latter case the

graphic method can render very great service. It fixes the characters of the tremors, and at the same time it unveils those that are simulated: after a little while irregularities are produced betraying the fatigue of the individual.

The graphic study of the respiratory apparatus is made by means of elastic bulbs placed upon the thorax. At each respiration these bulbs, which are fixed by a circular inextensible string, are compressed or distended, while the change in pressure produced in their interior is transmitted to a recording drum. Most of these apparatus, styled *pneumographs*, indicate the total expansion of the thorax. By using two separate bulbs, however, and two independent threads fixed upon the spinal column, a separate tracing for each half of the thorax can be obtained. This apparatus, designated as *bilateral stethograph*, furnishes exact indications as to the extent and form of the movements of each half of the thorax and reveals the slightest differences.

The graphic method is especially serviceable in the study of the circulatory system.

The movements of the heart can be directly registered by means of the *cardiograph*, which is essentially formed of a bulb provided with an exploring button communicating with the organ through the chest wall.

The arteries are more frequently explored. The *sphygmograph* is applied to the radial artery. The movements of the vessel are transmitted to a lever and are directly recorded upon a sheet of paper, which moves onward by virtue of a clock mechanism. In view of the fact that this apparatus furnishes somewhat varied indications according to the manner in which it is applied, the *sphygmometrograph* has recently been proposed. A very ingenious contrivance renders it possible to appreciate the pressure exerted by the apparatus upon the artery; the tracings are more exact, but the instrument is complicated and difficult to employ.

We shall not dwell upon the numberless other applications of the graphic method; various apparatus have also been made use of for exploration of many other organs. Thermometers have also been constructed which register the temperature of the body in a continuous manner. Finally, there is every reason to hope that by means of *chronophotography* and *cinematography* results as important will be obtained in pathology as have already been arrived at in physiology. Especially in nervous diseases attended by disturbances of the gait, the study of photographs taken successively at short intervals is evidently liable to lead to interesting deductions.

CHEMICAL PROCEDURES.—Chemical analysis furnishes clinical results of considerable importance. It is applied particularly to the

study of normal and pathological humours, such as the urine; less frequently to the gastric juice and exceptionally to the blood or accidental fluids, such as those of ascites, pleurisy, cysts, etc.

Chemical Analysis of the Urine.—Examination of the urine should be made in all cases and in all patients. When complete information is desired, long and delicate manipulations are required; in practice, however, there are certain investigations within the reach of all physicians which should never be neglected.

In the first place, the amount of urine voided in twenty-four hours is to be determined. For this purpose the patient should be instructed to collect his urine during a day and a night. The colour is readily appreciated; for exactness, recourse is had to the coloured scales published by Neubauer and Vogel. It is equally easy to determine the transparency, consistence, odour, presence of filaments, substances in suspension, or the existence of sediment. Furthermore, it is always well to ascertain the reaction and density.

If the urine is turbid, the cause of this anomalous state must be sought for. It is to be remembered that in most cases turbidity is due to the presence of mucus, pus, uric acid, urates, or excess of phosphates. Mucus is precipitated by acetic acid; pus forms a curdled mass by the addition of ammonia; uric acid and urates are dissolved by heat; phosphates become soluble by the addition of acetic acid.

When the urine is more intensely coloured than natural, the cause must be determined. Blood imparts to it a red or brownish hue; microscopic examination then demonstrates the presence of red blood corpuscles. In case of hemoglobinuria, recourse is to be had to the spectroscope, which shows the two characteristic absorption bands. The same instrument permits the recognition of urobilinuria. Finally, intense colour is often referable to the presence of biliary pigments. These are detected by Gmelin's test. A small amount of a mixture of fuming and ordinary nitric acid, in the proportion of 1 to 4, is poured into the tube containing the urine. When carefully poured along the wall of the tube, the denser acid falls to the bottom, and at the point of contact of the two fluids there is formed a series of superposed rings—green, blue, violet, and yellow. Only green is characteristic. In case the reaction is not sufficiently definite, the pigment should be dissolved by means of chloroform, and the latter, after having been decanted, should be treated with nitric acid. In some instances it is well to supplement examination of icteric urine by an inquiry as to the presence of biliary acids. For this purpose, Pettenkofer's test is employed. The addition of a certain amount of a solution of cane sugar, and then of a few drops of sulphuric acid, produces a violet-purple colour. Instead of pouring the acid upon the

urine, it is preferable to deposit a few drops of it upon a filter paper saturated with the icteric urine, to which sugar has been added.

These various tests are of practical interest; there is, however, an examination of greater importance which is required in all cases—namely, that for albumin and sugar.

For albumin, a trace of acetic acid or vinegar is added to the urine and then heated; or nitric acid is poured into the tube. Since the time of Gubler it is customary to pour the acid along the wall of the tube; the albumin, when present, forms above the acid an opaque white layer, and above this a ring of uric acid or urates appears. This procedure (*the contact method with nitric acid*) is insufficient. It is better to resort to more delicate tests. Tauret's test (iodo-mercuric solution) is altogether commendable. It is applied in the following manner: A small quantity of urine is poured into a test tube; the reagent is then added. If the urine remains clear, it can be decided that no albumin is present; if it becomes turbid, it must be submitted to heat before giving a decision. Three occurrences are then possible: (1) The precipitate may increase; (2) it may unite in the shape of small flocculi, and the liquid becomes clear; or, lastly (3), it may be dissolved by heat and reappear when cooled. In the first case, non-retractile albumin (Bouchard)—i. e., globuline—is present; in the second case, albumin is said to be retractile; it is a serine. Finally, when the specimen is cleared by heat, it is understood that the precipitate is due to peptone or alkaloids, and, in fact, questioning almost always proves that the patient has taken quinine.

The method just indicated is a most important one, because it reveals at the same time the presence of albumin, peptones, and alkaloids. It is objected that a precipitate may be produced by mucin; the error, if it is ever liable to occur, can be avoided by treating the urine with acetic acid, which precipitates mucus in the absence of heat. When pus is present, the urine is also albuminous; in this case the diagnosis is made in view of the turbid, opalescent, or milky appearance of the fluid, and by the use of ammonia, which produces a viscous, ropy, and even compact mass.

The quantitative analysis of albumin is clinically made by means of Esbach's tube (albuminometer), an inexact procedure, but sufficient for practical purposes.

We shall not dwell upon the examination for sugar and its quantitative estimation; the procedures are indicated in all treatises on chemistry and urology. In clinical examinations it generally suffices to look for sugar by Fehling's solution. For its quantitative analysis, Bouchardat's method is employed in the following manner: The specific gravity is found and the last two figures are multiplied by 2;

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the product is then multiplied by the quantity voided in twenty-four hours, and from the final product are subtracted 60 grammes, representing the other elements of the urine. It is hardly necessary to say that the result is but approximative.

Whenever glycosuria is met with, ethyldiacetic acid is always to be sought for. A few drops of perchloride of iron are poured into a tube containing the urine. The reagent, being heavier, goes to the bottom and assumes a characteristic colour—that of Bordeaux wine. A cause of error to be avoided is the presence of antipyrine, which gives an almost identical colour. If the patient has ingested sodium salicylate, the perchloride gives an intense violet colour which is quite different from the preceding.

In brief, clinical examination of the urine requires but a few re-agents—viz., nitric acid, Tarnet's reagents, the cupropotassic liquid, perchloride of iron, acetic acid, and ammonia. To these may be added hydrochloric acid, very useful for the detection of indican. The urine heated with this reagent becomes violet in colour.

Supplemental information is only exceptionally required. Quantitative estimation of urea, uric acid, chlorides, phosphates, and more rarely of sulphates or other substances, as the case may be, should then be made.

Examination of the urine may also inform us as to the activity of certain organs. As has already been stated (page 202), the state of the liver can be determined by the study of alimentary glycosuria. To appreciate the state of the kidneys, readily detectable substances, such as sodium salicylate, potassium iodide, and methylene blue (this colours the urine) are administered and then looked for in the urine. The urinary elimination is also of service in the study of the gastro-intestinal functions. Salol is given to the patient; so long as this medicine remains in the stomach the urine contains nothing of a special character; but when salol arrives at the duodenum, it undergoes decomposition, and gives off salicylic acid, which is absorbed and eliminated by the urine, where it is discovered by means of perchloride of iron. The motility of the stomach is thus appreciated.

Analysis of the Secretions and of the Blood.—For examination of gastric contents Günzburg's capsules are sometimes employed. A small fragment of potassium iodide is enveloped in a rubber bound with fibrine. When the latter is digested by the gastric juice, the rubber opens and the iodide, being absorbed, is readily detected in the saliva by means of starch and nitric acid. The time elapsed between the ingestion of the capsule and the appearance of the reaction indicates how long gastric digestion lasts.

More often, however, recourse is had to analysis of the gastric

juice, which is collected by means of a tube after a test meal. The procedures made use of are very complex; their main object is to appreciate the activity of the hydrochloric secretion and the state in which chlorine is excreted.

The chemical analysis of the sputum is seldom made. It is only necessary to know that chlorides abound in the expectoration of pneumonia; that a considerable quantity of cholesterine is met with in the same disease, while it is very rare in consumptives; and that the glycogenic substance is encountered in all purulent expectorations.

The chemical analysis of the blood requires too great quantities of the fluid to be practicable. However, with 2 or 3 cubic centimetres of blood some characters of interest may be appreciated—such, for instance, as the rapidity of coagulation, and especially the appearance of the serum, which, instead of being of the normal yellow hue, may have a milky look, or be greenish or reddish. The presence of bilirubin, hemoglobin, or urobilin in the serum can be recognised by means of spectroscopic examination. Finally, an excess of uric acid may be looked for by plunging a thread into the fluid after having added to it acetic acid in the proportion of 6 drops to 4 grammes. Within twenty-four to forty-eight hours the fluid almost completely evaporates, leaving upon the thread a deposit of characteristic crystals. The investigation of uric acid, so important for the semeiology of gout, is made more easily with the serum obtained by a vesicatory.

All these examinations, including that of the density, although possible with such small quantities of blood as to be without any inconvenience for the patient, are too delicate to enter the domain of current practice. The same is true of the analysis of pathological secretions or excretions. Chemical examination of vomited or fæcal matters is very seldom, if ever, undertaken, and is without importance unless it be in cases of poisoning. We shall not dwell upon this question, which is completely exposed in treatises on biological chemistry and legal medicine.

MICROSCOPIC EXAMINATION.—Excretions, blood, and at times tissues and pathological fluids are submitted to microscopic examination, and in this manner the presence in them of cellular or crystalline elements, parasites, and bacteria can be recognised.

In the case of urine, for instance, chemical examination must very often be supplemented by a microscopical study, the latter being of considerable importance in appreciating crystalline deposits. The blood corpuscles are readily recognised by their characters; it should, however, be remembered that the latter, being decolourized and swollen by the fluid, often assume a spherical form. When the urine is very alkaline, they are rapidly dissolved in it.

The presence of leucocytes is readily recognised: they are met with in all urines, but in small numbers; they are often found in the form of small masses in the filaments of chronic gonorrhœa patients.

Epithelial cells are also nearly always met with. Those coming from the bladder possess an irregular appearance, often recalling the form of a racket; those derived from the pelvis are pavemental; those of the kidneys are cylindrical or cubical. Cells of renal origin are not normally found. Under pathological conditions they are generally met with, isolated or united, along with *cylinders* (casts). The latter name is given to elongated productions, reproducing the form of uriniferous tubules, made up of hyaline or granular masses and epithelial cells.

Finally, microscopic examination likewise reveals the presence of spermatozoids in the urine, and, in case of tumour, fragments of normal or neoplastic tissues.

Microscopic examination of vomited matters is seldom made, and a little more frequently that of fæcal matters. Blood corpuscles, leucocytes, epithelial cells, and especially food particles are sought for, the presence of the last-named element being dependent upon a more or less marked disorder of digestion.

Microscopic examination is also applied to the semen, to detect spermatozoids, and to various exudates, to determine the presence of figurate elements in them, particularly of leucocytes.

Special attention should be devoted to sputa. Microscopic examination reveals their nature. The presence of epithelial cells, which are often altered and degenerated, is not of great semeiological significance. Small mucoid corpuscles, purulent or bloody globules, and cylindrical filaments of fibrine are often met with in expectorations. It is more important to look for elastic fibres, which can readily be demonstrated by means of acetic acid that leaves them intact, after having dissolved the other elements, or by means of eosine, which colours them intensely. Their presence means a destructive lesion of the lungs—e. g., abscess, cavity, or gangrene. In the last-named affection, however, they are often absent, for they can be digested by a special ferment originating in the sphacelated lung.

Sputa may also present to the microscope pigmentary masses and various crystals. In cases of putrid bronchitis or pulmonary gangrene, crystals of margarine and of cholesterine, leucine, tyrosine, at times ammonio-magnesian phosphates, and, after bronchial hemorrhage, hematoidine are met with. Particular crystals (the so-called Charcot-Leyden), occurring under the form of elongated and brilliant octahedrons, are encountered during and after a paroxysm of asthma.

Examination of the Blood.—The microscopic examination most frequently practised in clinics is that of the blood. By means of apparatus that are easily handled the richness of blood in red corpuscles can readily be determined. In France, the *hematimeters* of Potain, Malassez, Hayem, and Nachet are commonly made use of. The principle is always the same. A known quantity of blood is diluted in a preserving fluid and examined under the microscope in a well-calibred tube or cell. Under normal conditions the number of red corpuscles per cubic millimetre is from 4,100,000 to 5,000,000. Under pathological conditions these corpuscles may increase in number, though this is rarely the case. This condition is said to exist when, after large losses of liquid, particularly in cholera, the blood is more concentrated than is natural. The highest degree of hyperglobulia, however, is observed in congenital cyanosis.

Decreased number of the red blood corpuscles is far more frequent, and characterizes anæmic and cachectic conditions. Along with variations in number should be decided the qualitative modifications which are of greater consequence. The richness in hemoglobin must be carefully determined. To this effect various chromometers are employed, the simplest among them being that of Hayem. Two small cups are fixed upon a slip of glass; one is filled with a dilution of blood, the other serves to hold papers of various shades of red. It will suffice to find the shade corresponding to the dilution under examination, since the papers possess determined values. In this manner it may be decided that, in certain anæmias, the defect of the red corpuscles is not in the quantity but in the quality.

Microscopic examination also reveals the size of the corpuscles, which may be larger or smaller than normally, the presence of a nucleus (nucleated red corpuscles) in certain cases, and their deformities; they retain their biconcave shape, but their borders are often irregular and thickened, owing to the presence of pigmentary granulations.

Along with red corpuscles are found small elements designated as hematoblasts (Hayem). Their numbers are apt to increase suddenly after hemorrhages and at the end of acute diseases. They constitute one of the elements of the hematic crisis. Finally, globules may be seen united and agglutinated by a viscid substance: these are the so-called phlegmasic plates.

The study of the red corpuscles and of hematoblasts may be made in a very simple manner, without staining. The same is true of the white blood corpuscles when their number only is to be estimated. In other cases histochemical reagents must be resorted to. To-day it is not sufficient to simply decide that the number of the white

corpuscles is above or below the normal, their variety must also be determined—i. e., whether lymphocytes, mononucleated or polynucleated globules, or oxyphile or neutrophile basophiles are present.

Microscopic examination also reveals the manner in which coagulation of blood is effected. The fibrinous network characterizing coagulation may form too soon or too late. In phlegmasias coagulation is delayed, the fibrine has increased, the leucocytes and hematoblasts are more numerous than normally.

It can be seen by these few examples that examination of the blood renders great clinical service. It is always useful, but there are two cases in which it is indispensable: when anæmia is present or leucæmia is suspected. If the case is one of anæmia, examination of the blood is the only means of knowing whether the prescribed treatment produces any amelioration. In leucæmia it is impossible to make a positive diagnosis so long as the number of white corpuscles and their proportion to the red corpuscles are not determined.

Microscopic examination may detect the presence of parasites in the blood, humours, and tissues.

The filaria and the hematozoon of malaria are those most frequently found in the blood; the oidium is met with in the mouth; the *Aspergillus fumigatus* and actinomyces in the expectorations. Vomited matters and stools of course contain numerous parasites; it will suffice to mention the sarcinæ of the stomach, the amœbæ and *Anguillula intestinalis*, and often the ova of more highly organized parasites. Finally, microscopic examination, which is indispensable for the study of certain skin diseases, and particularly of tinea, is also applied to the investigation of parasites in the pus of abscesses and in visceral collections. When a fluid is suspected to be of hydatid origin, the hooklets, which are of great diagnostic value, must be sought for. Finally, when trichinosis is thought of, a small fragment of muscle, taken by means of a harpoon, must be submitted to microscopic examination.

BACTERIOLOGICAL EXAMINATION.—There are three methods for the investigation of pathogenic microbes: Microscopic examination, cultivation, and inoculation into animals.

Microscopic examination of the blood affords information in only one microbic disease—that is, recurrent fever—in which case Obermeier's spirilla can be seen during a paroxysm. In most other instances the blood contains no microbes, or too few, if any, to be detected in a preparation. The anthrax bacillus has indeed often been observed in the blood, but examination has then been made in that last stage when events of a grave character are present and the microscopic demonstration has no longer any clinical importance.

Microscopic examination 'suffices to determine the presence in pus of certain microbes difficult of cultivation, such as the tubercle bacillus and gonococcus. It is likewise serviceable in the case of certain species with peculiar morphology, such, for example, as streptococcus and pneumococcus.

The tubercle bacillus may be sought for in all exudates, especially in the expectorations, in the urine, stools, pus, and tissue *débris*. It is, however, to be borne in mind that, while the presence of the bacillus is of incontestable diagnostic value, its absence does not necessarily imply absence of tubercular lesions. When the microbes are very few in number they may escape notice. Hence, in examining the urine, care is taken, in laboratories, to first submit the liquid to centrifugation in order to bring together the scattered bacilli.

Microscopic examination is often resorted to for detecting in the expectorations the pneumococcus, which is readily recognised by its form, consisting of two elements and its capsule; the streptococcus, whose appearance under the form of a chain is characteristic; and the bacillus of Friedländer, a rod surrounded with a capsule. In most cases the microbes are so very numerous and varied that a simple microscopic examination does not warrant a positive conclusion. When, for example, it is desired to make examination of a false membrane derived from the throat, cultivation is indispensable for determining its diphtheritic nature. The same method of observation is applicable to the differentiation of microbes in fæcal matters.

Among pathological products pus is the most frequently examined under the microscope. The pneumococcus, streptococcus, staphylococcus, tetragenus, and gonococcus are then very readily distinguished. The last-named agent has, as is known, a peculiar form, and, unlike the other pus cocci, is decolourized by Gram's method. In these various pathological products actinomycetes may also be looked for. They are perceptible to the unaided eye when the suspected pus is spread over a glass slide, upon which they appear as small, slightly elevated granules. If the preparation is treated with picrocarmine, they appear under the microscope in the form of rosettes stained an intense yellow by the picric acid.

Cultivation.—The method of cultivation requires a quite complicated apparatus and special technical knowledge, and, therefore, can hardly be made available in ordinary practice. Nevertheless, it is often resorted to in various forms of angina. The majority of physicians are to-day convinced that clinical observation alone is powerless to distinguish the diverse varieties of sore throats, and particularly diphtheria. This statement is exaggerated and has led to manifest abuses. In reality, two instances are observable. In some cases

diphtheritic sore throat presents clinical characters so distinctive that doubt is rendered impossible, and the serum treatment should then be applied immediately. In the meantime bacteriological examination will show whether the diagnosis was right or wrong, but almost always it will confirm the clinical diagnosis, and therefore it is not indispensable from a clinical standpoint. At other times the sore throat, although pseudo-membranous, is so benign that the use of serum is not indicated. It is in such cases of medium intensity that cultivation renders great service, although attentive examination is very often sufficient. However, the clinical diagnosis of diphtheria requires long experience and is hard to acquire; hence, many physicians have adopted the bacteriological method, which appears to be simpler.

For the bacteriological examination of lesions suspected to be diphtheritic, the products are placed in a tube of gelatinized blood serum. In most cases the diphtheria bacillus develops within twenty-four hours and before all other microbes. The mere presence of colonies is not, however, sufficient to affirm the bacteriological diagnosis. Microscopic examination of the culture is indispensable.

Cultivation is sometimes resorted to for determining the presence of the pneumococcus in sputa. To this effect defibrinated coagulated blood is preferably employed.

The typhoid bacillus is sought for particularly in the fæcal matters. This is a very delicate procedure and requires long practice. The cholera vibrio is more readily discovered: cultivation is done in peptonized water, and at the end of twenty-four hours 5 to 10 per cent hydrochloric acid is added to the culture, when the red reaction, or cholera red, becomes manifest. Although this colour, which is due to the presence of indol, may be obtained with other microbes, it nevertheless possesses a certain value.

Cultivation of pus presents nothing special. Cultivation of the blood is made either by taking a drop of blood from the finger, or, what is preferable, drawing it from a vein by means of a well-sterilized syringe. In order to detect a microbe a great amount of blood must be sown upon appropriate media.

Serum Diagnosis.—Another bacteriological method, inaugurated by Dr. Widal, seems to render remarkable service. This method is based upon the fact that in certain diseases the serum acquires the property of agglutinating the pathogenic agent. A few drops of blood are therefore taken, and the generally diluted serum is mixed with the microbe which is to be studied. If the disease is really dependent upon it, the scattered individuals come together in small masses. This method, spoken of as serum diagnosis, was first employed in

reference to typhoid fever; according to the researches made by Dr. Arloing and his pupils, it also appears to be applicable to tuberculosis.

In brief, bacteriological diagnosis can be conducted in three ways:

1. Microscopic examination of contaminated parts, which constitutes an excellent procedure in cases of tuberculosis, recurrent fever, actinomycosis, and gonorrhœa, and is often sufficient for the investigation of the pus cocci.

2. Cultivation, which is used especially for detecting the diphtheria bacillus.

3. Serum diagnosis, applicable to typhoid fever.

INOCULATION INTO ANIMALS.—The last method consists in utilizing living animals. It is diagnosis by biological procedures. Recourse is had to this method when the microbe can not be detected by direct examination or cultivation. Such is especially the case with the pneumococcus and the bacilli of glanders and tuberculosis.

The liquid suspected to contain pneumococci is inoculated into a mouse. The animal succumbs within twenty-four to forty-eight hours, when its blood is found full of encapsulated diplococci having an altogether characteristic appearance.

The best procedure for the biological examination for glanders bacillus is that of Straus. The suspected pus is introduced into the peritoneal cavity of a male guinea pig. If the animal does not succumb to a peritonitis caused by an accidental microbe, an orchitis develops within twenty-four hours, demonstrating the presence of glanders.

The suspicious products of tuberculosis are likewise inoculated into a guinea pig. The fact that the period of survival is variable and at times very long renders the procedure scarcely practicable. Although the development of multiple adenopathies and emaciation of the animal suggest tuberculosis within ten days, granulations appear in the viscera only a month after inoculation.

The best means of making a diagnosis of hydrophobia is inoculation into animals. The autopsy of a rabid dog is negative; it reveals no lesions. Post-mortem diagnosis is, therefore, impossible unless a particle of the medulla be inoculated beneath the dura mater of a rabbit. Unfortunately, quite a long period elapses, from twelve to twenty days, before the symptoms become manifest.

The toxicity of certain normal or pathological fluids has also been studied upon animals. Blood serum or urine has more than once been injected. Toxicity of the urine is studied upon rabbits by means of intravenous injections; we have already spoken at length of the interest of this method, which, unfortunately, is not practical (page 200).

EXPLORATORY PUNCTURES AND INCISIONS.—Notwithstanding the numerous procedures of exploration above indicated, diagnosis is not always an easy matter. Explorative punctures and incision are therefore sometimes resorted to.

Exploratory punctures are done by means of a syringe provided with a capillary needle. It is possible to thus safely draw blood from a vein, cerebro-spinal fluid from the lumbar region, interstitial fluids from the liver and spleen, and exudates from the pleural cavity. In the case of muscular lesions a small punch or the harpoon of Duchenne de Boulogne is employed. Finally, biopsies are sometimes practised—i. e., a small particle of an organ or tissue is extirpated, generally a little piece of skin or of tumour. All these procedures serve to furnish material for microscopic or bacteriological examination. At other times puncture reveals the presence of liquid collections. Explorative punctures are thus made into various serous membranes, pleura and peritoneum, as well as into organs, such as the liver. The punctures reveal the presence and nature of fluids.

When puncture is inadequate, incision is resorted to. For instance, an exploratory laparotomy has for its object the exposure of the deep-seated organs, and, should any operable lesions be found, to then and there extirpate the diseased parts.

CHAPTER XXIII

DIAGNOSIS AND PROGNOSIS

Questions to be solved in making a complete diagnosis—Diagnosis of infectious diseases—Investigation of the previous state of the subject and of the multiple localizations of the infectious process—Importance of clinical types—Diagnosis of organic affections—Necessity of retracing the morbid series—Bearing of a complete diagnosis upon prognosis—Bases of prognosis—Examination of parts secondarily affected—Prognosis of actual manifestations—Prognosis for the future and for the descendants.

WHEN the patient has been questioned and thoroughly examined, having all his apparatus and organs systematically passed in review, a clinical conclusion should be arrived at. A diagnosis must be laid down—viz., the nature and causation of the present affection must be recognised and traced to the disease upon which it depends.

The questions to be answered are very numerous, and of course vary from one case to another. They can, however, be grouped in the following manner:

1. What are the present disturbances?

2. What is their immediate cause—viz., which organ or system are they referable to?

3. Are the affected parts involved primarily or secondarily? Are their disorders and lesions independent or due to a common cause? Among the organs attacked, which one was disturbed first and to which are the other manifestations subordinate?

4. The connections of the present disturbances being disclosed, is it an affection or a disease that is to be dealt with?

5. If an organic affection is present, can the disease of which it is a sequel be traced?

6. What is the nature of this disease? What position does it occupy in nosology?

7. Upon what sort of constitutional ground has it evolved? What will be its ulterior evolution?

To fix these ideas, let us first consider the infectious diseases.

In this case, after having made a complete examination of the patient, the physician finds himself in a position to answer the questions raised by the diagnosis. If he can not always arrive at precise conclusions, he can at least closely approach a solution. In the beginning of the disease there may be some doubt, but hesitation is only between two or three hypotheses, and, in general, after a day or two, further developments lead to an exact and conclusive diagnosis.

For example, a child or a young man is suddenly taken with a sore throat; there are fever, a rapid pulse, coated tongue, and a red throat with some whitish exudation upon the tonsils. There is obviously an acute angina. But what is the nature of this angina? To determine this is more difficult; the question, however, is of the greatest import from the standpoint of prognosis and treatment. The sudden onset, the pultaceous appearance of the tonsillar deposit, and the plainly inflammatory reaction warrant the exclusion of diphtheria. But, then, is it a simple or a scarlatinous angina? The age of the patient, the severity of the fever, the intense redness of the throat, the rapidity of the pulse, and at times the existence of a concomitant epidemic, point to scarlatina. A positive diagnosis, however, is impossible before the third day, when the appearance of the eruption will permit a decisive conclusion. In this case a symptomatic manifestation of the first importance for the diagnosis was lacking.

In other instances a positive diagnosis can be made from the start, even though no sign seems to justify it. For example, a child of eight or ten years is suddenly attacked by intense fever; it is found dyspnoic, tormented with a small dry cough, its face is flushed, its cheeks are red, and the temperature is at 40° C. Although auscultation gives a negative result, pneumonia is diagnosticated, and, in fact, within twenty-four hours, sometimes two or three days later, the characteristic tubal murmur is heard. Owing to a little clinical experience, the diagnosis was positively made from the start, notwithstanding the absence of stethoscopic signs, and despite the presence, in certain cases of nervous phenomena or even convulsions, which would at first suggest meningitis.

Illustrations could easily be multiplied. These few facts suffice to show that in the majority of infections a diagnosis can be laid down after a minute and systematic examination of the whole organism.

Recognition of the nature of the disease does not terminate the task. A man, for instance, is suddenly taken with chills, followed by pain in the side, painful coughing, rusty expectoration, and intense fever. On auscultation, a focus of crepitant râles or tubular murmur is found in one of the lungs. The state of the lung accounts for all the disturbances, and the evolution of the disease leads to the affirma-

tion that we are in the presence of an infection—i. e., pneumonia. All the questions requiring a solution are thus answered except the last one. In this instance, to make the diagnosis of pneumonia was not a task of difficulty; but to determine the constitutional ground upon which the infection runs its course is a more delicate question. With this object in view, the patient must be carefully questioned with reference to his morbid antecedents, both personal and hereditary. Besides, all his viscera must be attentively explored. It is something to have diagnosticated pneumonia by auscultating the lungs, but a physician should never be contented with so summary a diagnosis. The whole prognosis and treatment will spring from the knowledge he is able to acquire as to what sort of constitution the pathogenic agent has to deal with and as to which organs are involved. Only after having appreciated the previous and concomitant symptoms will he be able to arrive at a complete diagnosis and to predict the evolution of the disease. In case the subject is young and vigorous, recovery is the rule; when an aged person is attacked, the termination is generally fatal. In these two instances pathology appears to furnish sufficient information. Take, for example, another patient, vigorous in appearance, attacked by pneumonia. It might be thought that he also will recover. However, in making a systematic examination of the organs and analysis of the urine, a lesion until then in a state of latency—e. g., a cardiopathy, cirrhosis, albuminuria, or glycosuria—is discovered. A quite different evolution is therefore expected in this case, in which the situation is thoroughly comprehended, owing to an exhaustive, carefully conducted examination.

The example above given is a simple one. Furthermore, it may be stated that an infectious disease is diagnosticated with relative facility. The question is one of fresh acute evolution, all the stages of which are followed and which has come under observation shortly after the onset. In most cases diagnosis can be arrived at if the pathology is well studied. The only point of consequence is to make a complete diagnosis—viz., to determine the constitutional soil upon which the disease is developing and the organs disturbed. In fact, it is known that morbid manifestations are more diffuse than was formerly believed. The microbic toxines affect the entire economy, and the task of the clinician is to make out what parts are involved and to what degree they are affected. It may be again stated that to find the name under which the disease should be designated is relatively easy; the mere diagnosis, however exact it may appear, is incomplete, inadequate, and responds only to the first, the easiest, and the least important part of the problem.

With the view of facilitating the physician's task, nosologists have taken care to indicate a certain number of clinical forms in infectious diseases.

Taking typhoid fever and pneumonia as examples, it was shown (page 374) how, in view of either the patient's state, or of the general disturbances, or of the localizations, the various types could be classified and practical indications derived. The types, however numerous, do not, of course, respond to all clinical modes and their innumerable variations; they do, nevertheless, furnish valuable elements of prognosis and treatment, and should therefore be very carefully studied.

In certain instances the complexity of the clinical form results from the coexistence of various manifestations or multiple localizations, the relations of which one to another are not easy to determine.

Thus, for example, in a patient suffering from erysipelas a pulmonary blowing murmur is perceived at a certain moment. Is it a case of pneumonia with streptococci—i. e., a visceral localization due to the agent which has caused the primary disease? Or are we in the presence of an infection referable to a superadded microbe—viz., pneumococcus? Both varieties of pneumonia have been observed in cases of erysipelas, and it is impossible to make a differential diagnosis without bacteriological examination.

The difficulty is greater when the pathogenic agents are unknown. In a child presenting a scarlatiniform eruption along with other infectious phenomena, how is it possible to decide whether there is merely a rash rather than a true scarlatina? It is right to hesitate even when multiple arthropathies become manifest in a scarlatinous patient arrived at the period of convalescence; are they to be ascribed to the scarlet fever or are they dependent upon a concomitant acute articular rheumatism? The doubt is often inevitable in such questions. In the absence of a positive criterion, only hypotheses can be put forward with regard to these morbid associations.

The difficulties are still greater when the history of an organ affected is to be traced.

Let us first consider a man suffering from intense dyspnœa, accompanied with œdema of the lower extremities and pain in the right hypochondrium. The present symptoms are easily explained by clinical examination. In fact, fine râles are found in the lungs, albumin in the urine, and hypertrophy of the liver. Have the organs been affected independently of each other and attacked primarily? This hypothesis is not admissible, because, by examining each organ one by one, a systolic murmur is perceived at the apex of the heart, with irregularity in the beatings, and unequal and false steps in the pulse.

On the other hand, it is learned by questioning the patient that he once had an attack of acute articular rheumatism. It is then easy to determine the connections of the clinical phenomena. The present symptoms are dependent upon pulmonary, renal, and hepatic disorders, and the latter are referable to a cardiopathy—i. e., an organic affection which is itself nothing but a sequel of the acute articular rheumatism, an infectious disease.

It should not be believed, however, that the phenomena can always be connected in so simple and so evident a manner. An evolution almost similar to the one just referred to can be discovered, the occurrences having their origin in the lung. Take, for example, a man suffering with asthma from childhood, whose lungs have become emphysematous as a result of repeated dyspnoic paroxysms; these organs have secondarily produced dilatation of the heart, and the cardiac insufficiency is responsible for the hypertrophy of the liver and the renal lesion with its double consequence—viz., albuminuria and œdema of the lower extremities. The connections of the morbid occurrences can only be disclosed by minute questioning and precise appreciation of each disturbance.

Instead of the lungs, the kidneys may be primarily altered and have occasioned cardiac dilatation with all its consequences. So may the liver be primarily diseased and influence the other organs.

In this manner the same parts of the organism are finally affected, but the course of the events varies. Prognosis is quite different from one case to another, and treatment can not be the same.

Despite all the care that can be taken in examination, it is not always possible to trace exactly the succession of morbid occurrences; in an organism in which most of the viscera are affected, the respective subordination of the manifestations can not be determined when their course and chronological appearance remain unascertained.

Contrary to what is often stated, no particular gift, no sort of divinatory quality is required for classifying and interpreting the symptoms. The art of making a diagnosis is not inborn; it is acquired by the theoretical study of pathology and by repeated examination of patients. It is by virtue of having observed dissimilar morbid states that the aptitude for correct interpretation of disturbances is formed. Indeed, clinics show us far more complex cases than the study of pathology leads us to suspect. The didactic treatises can give no more than schematic descriptions. They consider diseases in their fundamental and constant elements, disregarding the constitutional soil upon which they evolve. But it is owing to the great variability of this soil that clinical types are so numerous and varied, and the physician must therefore appreciate the soil upon

which the disease or affection which he observes is developing, since upon that appreciation will he mostly base his judgment of the further evolution.

It is often repeated that it is well to resort to the physician who has been your doctor for many years, for he knows your temperament. The idea is right, but the reason is false. Long acquaintance is by no means necessary for the physician to appreciate the pathological value of an individual. He can appreciate it by careful questioning and thorough examination. The age, sex, family and personal antecedents, and previous affections or diseases should be considered. Such lesions or taints which may have been left by previous pathological occurrences must next be sought for. This also is a sufficient reason for always submitting a patient to a thorough examination.

When the present state, resisting power, and reactionary aptitude of the patient are exactly determined, and the functional energy and alterations of his organs are made out, then, and then only, is it possible to predict the evolution of the morbid process under observation. To answer this last question is to lay down a prognosis—that is, to solve the most difficult and important problem in medical art.

There are some diseases with a nearly determined evolution. In such cases the prognosis is derived from the diagnosis. Tubercular meningitis, icterus gravis, acute glanders, hydrophobia, and cancer are always, or nearly always, fatal. On the other hand, varicella, mumps, herpetic angina, and simple pneumonia in children almost invariably terminate in recovery. Nothing, it seems, could be simpler. Even in these cases, however, exceptions are met with: varicella at times proves fatal, and not a few distinguished physicians assert that tubercular meningitis is curable. It may be objected that these exceptions should not be taken into account. Leaving these facts aside, therefore, let us consider a case of frequent occurrence. When in the presence of a disease with variable prognosis, where are the elements of appreciation to be found? In statistics? It is theoretically known that pneumonia is fatal in a proportion of 10 to 20 per cent. In the face of a particular case, if he consults his numerical memory, the physician will declare that the chances of recovery are from 80 to 90 per cent. These figures are not without interest, but what is important to know is whether the individual under treatment will enter into the 80 cases that recover or into the 20 cases that die. In this respect statistics are hardly of any use. They may indeed show that the death rate is very high for the aged and almost nil for children; it suffices, however, that a few of the aged recover and some of the children succumb in order that we be compelled to look elsewhere for the basis of our appreciation.

In certain instances prognosis is self-evident. There exists such an *ensemble* of symptoms as to leave no room for the slightest doubt, as is the case, for example, with tuberculous or cancerous patients in an advanced stage of cachexia, and cardiac patients at the last period of asystole. In such cases the only delicate point is to know how long life may still be prolonged.

The greatest difficulties are experienced in those grave cases the termination of which must be foretold. In the first place, it should be borne in mind that the subjective sensations of the patient are often deceptive. The euphoria of cardiac, and especially of tubercular patients, even at an advanced period of the disease, is a familiar fact; on the other hand, reactions of great violence may break forth in certain predisposed individuals and mislead to a gloomy prognosis. Delirium, for example, is often more alarming than grave. On the contrary, certain affections, although well endured, are of very serious prognosis. Some pleuritic patients suffer from intense dyspnœa from a small amount of exudation, while others breathe in an almost normal manner with a pleural cavity filled with fluid. The manifestations experienced or even presented by the patient are, in fact, far more dependent upon his personal aptitudes than upon the state of the disease. They may, therefore, lead to error.

This remark does not imply that no value is to be attached to these various disturbances; ground should be taken, however, not upon a phenomenon, but upon the *ensemble* of manifestations. According to this principle, the various clinical types have been created in nosology, and, although there is as yet no absolute certainty in this respect, the prognosis of clinical forms is already tolerably well determined by pathology.

In order to arrive at more positive conclusions, greater importance should be attached to the state of organs or parts secondarily affected than to primary or principal localizations.

There is an example which can not too often be cited—namely, that of pneumonia. Examination of the lung is of the greatest importance for the diagnosis, but not so for the prognosis; at all events, those parts of the pulmonary apparatus which are most important to consider are not precisely those occupied by the primary lesion; the tubal murmur is of no great consequence. An element of greater weight is congestion extending beyond the hepaticized zone. And the other organs are to be considered more than the lungs. For example, the heart plays the first rôle in pneumonia; excessive rapidity of its pulsations, its weakening, and the occurrence of fœtal rhythm are of far greater consequence than the extension of the pulmonary process.

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Analogous reflections are applicable to tuberculosis. From a diagnostic standpoint the pulmonary localization possesses considerable importance, but is of little interest with reference to prognosis. The latter may be favourable even when the lesions have advanced and part of the apex is already excavated. The prognosis is to be deduced from the state of the other parts of the respiratory apparatus, and especially from auscultation of the bases. It will be indicated more particularly by accompanying phenomena—e. g., rapid emaciation, digestive disorders, albuminuria, and fever. These are the most significant manifestations. It would be easier and safer to make the prognosis without auscultating tuberculous subjects than to be guided simply by the data of stethoscopic examination.

A last, but not least, example is furnished by cardiac pathology. The prognosis of an asystolic paroxysm is more safely drawn from the state of the other parts of the organism than from that of the heart itself. Why are some asystolic patients so readily re-established under the influence of digitalis while others are not at all benefited by the same drug? The state of the heart is, of course, very important in this connection. The effects are entirely different according as the myocardium is or is not degenerated. At an advanced period, however, cardiac alterations are far from adequate to account for all. The fact is that the repeated attacks of asystole have given rise to cardiac cachexia; therefore the drug that acts upon the heart is powerless in an organism succumbing to consecutive alterations of other viscera—liver, kidneys, and lungs.

It is evidently impossible to lay down general rules of prognosis, since the modifications are too considerable from one case to another. The few illustrations above described give a tolerably clear idea as to how the evolution of diseases can be predicted. Prognosis, however, is far from complete when it does no more than predict whether the individual will die or recover from the attack under observation. Prognosis must answer the following three questions: (1) What will be the termination of the present disease? (2) What is its bearing upon the future of the patient? (3) Of what importance is it for his descendants?

It should, therefore, be determined whether the disease will be cured without leaving appreciable traces, and whether some disturbances will not persist in consequence. It should be decided whether relapses or recurrences are apt to take place, and whether they can possibly be guarded against. It should also be predicted whether there will be any sequel manifesting itself in the remote future, or whether the descendants of the patient will be liable to suffer from inherited effects of the attack; in other words, whether the disease

will for some time after its termination, or forever, expose the individual to the danger of begetting malformed, degenerated, or diseased offspring. Along with the prognosis of the individual the prognosis of the race must be laid down.

Then, and then only, has the physician answered all the questions which incessantly meet him on confronting every patient.

In order to arrive at a positive prognosis, ground should be taken upon the clinical examination of the patient, including the study of his antecedents, the state of his organs, and analysis of the urine. As to scientific procedures, they have thus far remained without importance. It was for a moment believed that bacteriology would supplant clinical observation. The study of diphtheria led to the erroneous conclusion that examination of cultures permitted one to determine the gravity of angina even in the absence of clinical observation of the patient. If the diphtheria was found to be uncomplicated, and if the bacillus developing upon the serum medium was not too long, the prognosis was favourable. If, on the contrary, the bacillus was long and mixed with numerous streptococci, the prognosis was grave. Although such correspondence may at times be observed, it far from constitutes the rule, and can not replace examination of the sick, or even modify the clinical prognosis made by the attending physician.

We likewise believe that no practical information can be derived from inoculations into animals. Besides the difficulties of the method, the results are too variable to be taken as a basis of prognosis. A microbe virulent for man not infrequently proves inoffensive for animals, and *vice versa*. Finally, Dr. M. P. Courmont has recently proposed an ingenious and interesting method of serum prognosis, but one which is too recent to enter immediately into practice.

En résumé, it may be said that, in the present state of medical science, prognosis as well as diagnosis should be based upon a thorough examination of the patient, and upon a systematic exploration of all his organs and apparatus. Although certain recent methods render great service to the physician, these are only the exceptions. The art of medicine can be practised by simple procedures, aided by the science of pathology, which requires long study, and by clinical experience, which can only be acquired after great and extensive practice.

CHAPTER XXIV

THERAPEUTICS

Division of therapeutics—Symptomatic therapeutics: its usefulness—Etiological therapeutics; antiparasitic and antiseptic medication; bacteriotherapy — Pathogenic and physiologic therapeutics; mechanical procedures; antitoxic medication; opotherapy; serum therapy—Modifications of nutrition and of nervous reactions—Hygiene and prophylaxis—Vaccinations.

THE object of medicine being to relieve and cure, all our efforts should tend toward therapeutics. Previous studies, the examinations to which the patients are submitted, and investigation of symptoms, pathogenic or physiological processes, and etiological conditions would be absolutely sterile and illusory did not all these serve to favourably modify the morbid evolution.

As has already been stated, therapeutics may be divided into four classes according to the principles upon which it is based: Symptomatic, etiological, pathogenic, and physiological therapeutics.

Symptomatic therapeutics remedies immediate disturbances and combats certain disorders without reaching their cause or reascending to their point of departure. Although in most cases symptomatic therapeutics is insufficient, and is often an acknowledgment of our ignorance, it is at times the only possible or admissible method. In the presence of symptoms threatening death, recourse must be had to urgent treatment which is directed to the disturbance observed, without reference to its origin. When an individual is attacked by grave hemorrhage, it would be ridiculous to waste time in studying its etiology or pathogenesis; no matter why and how the blood flows, the thing to be done forthwith is to arrest the bleeding; symptomatic treatment is the only rational one.

Likewise, when a physician is called to the side of an asphyxiated patient, recognised by the characters of suffocation dependent upon laryngeal stenosis, whatever may be the cause of the latter, his first thought is to re-establish the course of the air, and he immediately performs a tracheotomy. After this is done, there will be time to look

for the cause, and, if possible, to act upon it—i. e., to resort to a more rational medication.

Symptomatic therapeutics may serve as an auxiliary one, and is then perfectly justified. A patient suffering from syphilitic cephalalgia must receive specific treatment. However, as the latter requires several days to produce its effects, symptomatic medication is at the same time to be resorted to in order to assuage the nocturnal exacerbations of pain and procure rest to the sufferer. To this end, along with 4 or 6 grammes of potassium iodide directed to the syphilitic element, sulphonal or chloral hydrate should be prescribed to relieve the headache. Tuberculosis furnishes another illustration. Creosote and its derivatives are still the best medicines for combating this terrible infection; while administering them, however, a symptomatic treatment should also be made, by giving atropine for the sweats, opium for the cough, antipyrine for the fever, etc.

Finally, there are cases in which, despite profound examination, the physician can not discover the causal disease; he observes a symptom, and, being unable to connect it with its origin, he makes an attempt at combating it. He often succeeds in doing this and accomplishes a cure. Symptomatic medication then proves to be adequate. Laymen constantly practise according to this method, and, for want of a better, physicians also resort to it by curing, for example, diarrhœa by bismuth, constipation by purgatives, cough by opiates, neuralgia by quinine, antipyrine or phenacetine, etc. They do not know the cause of the diarrhœa, constipation, cough, or neuralgia; however, by combating the symptom, they overcome the disorder.

Symptomatic medication thus enters the domain of rational therapeutics when it remedies pressing disturbances or aids a causal medication. It is a confession of ignorance when employed as an exclusive method, or is directed to combat a disorder the causation of which remains undiscovered.

When we are able to trace the reactions of the organism to the prime cause which has called them forth, and when we can reach it, we employ *etiological therapeutics*. This mode of therapy appears at first to be the most rational. It would obviously seem that the suppression of the cause should result in the disappearance of all the consecutive disturbances. This is the application of the old adage: *sublata causa, tollitur effectus.*

This medication, however, is often impossible, and even useless. It is impossible when the cause can not be reached; it is useless when the cause has produced secondary disturbances evolving on their own account, and which may become predominant or persist alone. We should recall here our fundamental distinction between disease and

affection: in *disease,* etiological medication is often efficacious; in *affection,* it never is.

Thus, for instance, acute articular rheumatism is an infection which may be cured by a specific medication—sodium salicylate. This substance probably acts upon the very cause of the malady. Later on, when acute endocarditis is produced as a result of the acute process, etiological medication would be illusory: then the salicylate has nothing to do; the cardiac affection has an autonomous evolution and retains no specific character whatever from its origin. We must treat not the rheumatism but the cardiac affection.

It has been stated the primordial causes of diseases are divisible into four groups, according as the agent is a mechanical, physical, chemical, or an animate one. With mechanical causes, etiological medication is rarely useful, since such causes have but a transitory action. There is only one exception—that is, when a foreign body has remained in a wound: to remove it is evidently etiological treatment.

The action of physical agents is also transitory, except in the case of unhealthful climatic influence. To advise a patient to change the climate which does not suit his constitution is to practise etiological medication.

There is far oftener occasion to act upon chemical causes. An individual swallows a poison, and it is believed that the poison has not yet been completely absorbed; therefore, washing out the stomach with water containing, if possible, a substance capable of neutralizing the toxine is immediately resorted to. Thus an attempt is made at suppressing or at least diminishing the pathogenic action.

The study of parasitic diseases furnishes the best examples; its results are the best triumphs of etiological medication.

A child has an attack of convulsions. If symptomatic medication is thought to be sufficient, in this case, bromide, chloral, asafœtida, and the like are prescribed. The disorders will disappear only to reappear a few days later; they will again be arrested under the influence of the same treatment, but only for a short time. If, however, investigation being pushed further, the cause of the convulsions is looked for and found—for example, that the child has intestinal worms—a vermifuge is then administered, and the convulsions disappear in a definite manner.

Removal of the Medina worm, ablation of an hydatid cyst, the use of germicidal or antiseptic salves or solutions are as many examples of etiological medication.

It is to be noted, however, that in many cases the procedure resorted to is highly complex. When, for example, oidian stomatitis is treated by means of bicarbonate or borate of sodium, the medication

is not, as was once believed, etiological, since the parasite of aphtha thrives perfectly in an alkaline medium. The substances employed exert an indirect influence—they improve the state of the mucous membrane, and thus favour the destruction of the vegetable.

When an infectious agent is to be combated, etiological medication can be applied by means of antiseptics. The method succeeds when it is desired to disinfect a surface or an easily accessible cavity. Its application is more difficult when deep-seated cavities are to be treated. It can, however, be employed either by means of inhalations of antiseptic vapours, in the case of the respiratory passages, or by the ingestion of insoluble substances in the case of the digestive canal. The use of menthol inhalations in the former instance, and that of naphthol, benzonaphthol, betol, or salol in the latter, renders real service. Several authors believe that it is possible to go farther and contend that various substances, especially tannin, are capable of rendering the internal medium antiseptic.

Possibly, though not certainly, the so-called *specific* medications are of an etiological order. Mercury or potassium iodide given in syphilis, quinine in malaria, sodium salicylate in rheumatism, and potassium iodide in actinomycosis perhaps exercise a destructive action upon the known or unknown agents of these diseases. It may just as well be argued, however, that these medicines exert their effect upon the organic cells by increasing their resistance.

The desire of reaching the animate cause of infectious diseases has given rise to many methods. Besides antiseptic and specific medications there is *bacteriotherapy*, which consists in combating a pathogenic microbe with an inoffensive one. For instance, inhalation of *Bacterium termo* cultures are prescribed for consumptives. The results have not, however, been encouraging. The soluble products have then been resorted to. It was long ago noticed that an intercurrent erysipelas could improve a cutaneous tuberculosis. Hence the attempts at treating lupus by means of sterilized cultures of streptococcus, the action of which was re-enforced by the addition of a few drops of an equally sterilized culture of *Bacillus prodigiosus*. In some instances improvement has been obtained; the dangers, however, to which the use of microbic products exposes the patients do not seem to be compensated by the results. It has not been demonstrated that the effects of this toxibacteriotherapy are due to action upon the specific bacillus; it is even more probable that there is simply stimulation of the reactional activity of the organism.

Anticancerous bacteriotherapy is doubtless to be understood in the same manner. The injection of living cultures or of a mixture of the toxines of streptococcus and of *Bacillus prodigiosus* (Coley's method),

has afforded some interesting results, especially in the treatment of sarcoma.

The method is likewise etiological when *germicidal serums* are employed. This is a variety of antiseptic treatment, since a substance is introduced which is highly toxic for the microbes, very slightly so for the individual.

Finally, certain abortive treatments are to be included in the group of etiological medications.

Abortive medication may aim at three ends: to arrest a disease while yet in its prodromic stage, to prevent a disease from passing from one stage to another, and to cut short a morbid evolution.

In the case of gonorrhœa is found an example of abortive medication employed at the prodromic period. At the moment when a slight discharge of mucus begins, while the gonococcus is still in the superficial parts, the injection of a somewhat strong antiseptic may destroy the pathogenic agent. The method is abortive when the uterus is curetted in the beginning of puerperal fever; the cause of the disease is thus acted upon, since the uterine mucous membrane is, so far as is possible, freed from the streptococci invading it.

In the examples just chosen medication was of an etiological order. When abortive treatment is applied to a disease which has already been evolving for a more or less long period, the procedures employed are more complex. The cause is then less easily accessible and the action of therapeutic measures is brought to bear rather upon the diseased organism. This is pathogenic or physiological medication.

Pathogenic medication derives its guidance from the mode of action of the causes. The latter may act in two different ways: mechanically or chemically. They give rise to two forms of reactions—namely, nervous reactions and nutritional disturbances—the study of which constitutes pathological physiology. To these four modes of action and reaction correspond four therapeutic methods.

To mechanical causes are generally opposed *mechanical treatments*. In case of traumatism, simple mechanical procedures are employed to assure hemostasis, extraction of foreign bodies, coaptation of separated parts, and the maintenance of fractures. When the mechanical causes are of an internal order, the principles are the same. In cases of pleural, pericardial, or abdominal effusions compressing the subjacent organs and embarrassing their function, the indications are quite plain—namely, evacuation of the fluids. Likewise, in case of a strangulated hernia, intestinal occlusion, or obstruction of the bile duct, the physician endeavours, by mechanical means and surgical intervention, to stop the compression and suppress or remove the

obstacle. Mechanical procedures are also resorted to in cases of displacement of organs, hernia, eventration, and ptosis.

The procedures are often difficult of realization; intervention may be extremely delicate, but the indications are very simple.

Of the causes acting chemically, *toxines* are the most important.

In treating an individual who has swallowed a poison, the first indication is to wash out the stomach, thus removing along with the yet unabsorbed part of the toxine a certain amount of the same already eliminated by the gastric mucous membrane. In view of this fact lavage may be resorted to even when the poison has been introduced subcutaneously, as is often the case in morphine poisoning. At the same time physiological medication must be employed, which consists in favouring elimination through the various emunctories: purgatives, enemata, and diaphoretics are prescribed. Renal secretion particularly must be encouraged by the use of copious diuretic and hot beverages, and by subcutaneous or intravenous injections of salt water, with or without bloodletting. It is well to note that of these means some have a complex action. For instance, bloodletting does not act merely as a means of removing the poisons accumulated in the blood; it also modifies the phenomena of absorption and excretion by diminishing the blood mass. If the poison is not yet completely absorbed, bloodletting may hasten its penetration, and thus prove extremely harmful. We say " may," since this opinion is based upon an old experiment of Magendie. This author noticed that bloodletting favoured the toxic action of nux vomica introduced into the stomach; he thought that penetration into the blood was facilitated by the fact that the organism drew water to replace the loss of blood. The conclusion is acceptable, but, in order to be fixed, it requires new investigations, as the experiment is indeed highly complex.

In cases of auto-intoxication bloodletting can be resorted to without hesitation. It is daily practised with success upon uræmic patients. It serves to throw out with the blood a certain amount of the circulating poison, and, at the same time, through the osmotic current which it establishes from the tissues toward the blood, to prevent the accumulation of toxines in the tissues.

If it is feared that bloodletting will weaken the patient and, by reducing the blood mass, diminish the renal secretion, injections of artificial serum should at the same time be resorted to. The latter act by favouring the elimination of crystalloid substances, which pass more easily through the kidneys, and especially by stimulating the nervous system, the dynamogenic power of which is increased. This form of medication is therefore a complex one, and it effects more than a simple washing of the organism.

Neutralization of toxic substances may also be aimed at. This is very readily done when the poison is ingested. If it is an acid, then some alkaline solution, preferably a water charged with calcium or magnesium salts, is introduced into the stomach; there is some chance of thus forming insoluble combinations. If the ingested poison is exactly known, the medication can more readily be formulated. A substance capable of precipitating the toxine must be employed; the calcium salts, for instance, in case of oxalic or sulphuric acid; sodium chloride in case of silver salts; and tannin in alkaloidal poisonings. We shall not dwell upon these indications furnished by the study of elementary chemistry.

In order to relieve the pain and thirst of the patient, milk is often prescribed, this liquid possessing the additional advantage of being a diuretic. It is well, however, to remember that the use of milk may produce harmful effects; when the patient has swallowed a poison which is soluble in a fatty substance, as is phosphorus, milk hastens the development of disturbances; it should therefore be forbidden, and substances which favour oxidation should be prescribed, such as turpentine.

Neutralization of the poison is possible even when it is introduced subcutaneously. The action of venoms is very often arrested by means of various substances, such as potassium permanganate and hypochlorites.

If the poison has been absorbed and has penetrated into the organism, can its effects be neutralized? This is believed to be possible by means of antidotes.

The *antidote*, such as was conceived by old authorities and as is still understood by several at the present day, does not exist. To be real antidotes, the substances should mutually neutralize the effects of each other, or, in other words, exert upon the organism influences diametrically opposed. The fact is, however, that between poisons there exist only partial antagonisms or influences which can be neutralized by a complex mechanism. It is stated, for instance, that atropine and morphine are two antagonistic substances; it is true that they have contrary effects upon different apparatus. Yet one is not the antidote of the other, since death is produced far more rapidly by injecting a mixture of the two poisons than by the injection of but one of them. Atropine is also said to be the antidote of muscarine. Atropine paralyzes the extremities of the pneumogastric nerves and suppresses the inhibitory action of these nerves upon the heart. Muscarine arrests the heart by acting upon the pneumogastric; it will therefore have no influence upon an atropinized animal. But this is a case of physiological antagonism and in no wise one of antidotism.

Therapeutic serums are at times considered as antidotes: the antidiphtheritic serum is said to neutralize the diphtheritic poison as an acid neutralizes a base. Such was Behring's view, but it is not correct. The serum acts, not by destroying the poison, but by increasing the resistance of the organism. Serum therapy is not an antidotal but a pathogenic and physiological medication.

What is now generally designated as *opotherapy* (organotherapy) may perhaps be considered to be for the most part antidotal. It is well known in what it consists. When an organ is altered or suppressed, the patient is given the extracts prepared from the same organs taken from animals. Brown-Séquard, who initiated this therapeutic method, prescribed subcutaneous injections of testicular juice; he thus supplied the organism with the internal secretion which the testicles seem to elaborate for the stimulation of the nervous system. At the present day the thyroid gland is mostly used, which, when ingested or injected beneath the skin, effects marvelous results in myxœdema and in certain cases of obesity. Some encouraging results have been observed with the extract of liver in ovariotomized women.

Although antidotal medication in the old sense is no longer admissible, it is not impossible to favour the destruction and transformation of poisons. Certain medicines transform toxines into harmless substances; others exert an indirect influence by stimulating the activity of organs which are capable of annihilating or, we could almost say, digesting the poisons. Special therapeutic effort should be devoted to the liver, for it is demonstrated that the ingestion of sugar or of small doses of ether constitutes an excellent means of stimulating this organ and of increasing its action upon poisons, and its destructive power upon microbes. Finally, along with substances neutralizing toxines should be placed those which, by rendering them more soluble and dialyzable, favour their excretion. This method is most frequently applied to the treatment of auto-intoxication, and it is realized by the use of oxidants.

It has several times been stated that when the disease appears to be terminated, and the poison which gave rise to it is eliminated, the organism is not completely restored to its normal state. The persisting disturbances may be too slight to demand attention, while in other cases they may be evidenced by a series of nutritional modifications which are always consecutive to toxic, exogenous, autogenous, or infectious influences, and may be transmitted by heredity.

The disorders of nutrition are divisible into two types, according as the exchanges are accelerated or diminished. In the former case the nutritive process should be moderated, as is realized by means of so-called sparing (or economizing) medicines, such as arsenic and

valerian. In the latter case the nutritive movement should be stimulated; to this effect the salts of Carlsbad, Vichy water before meals, or potassium iodide in small doses, 20 centigrammes daily, are prescribed, along with cutaneous stimulations, douches, massage, and dry frictions; finally, the elimination of incompletely oxidized or poorly soluble substances should be facilitated by the administration of lithine and piperazine, which dissolve uric acid, and by sodium benzoate, which favours oxidation.

Of these various therapeutic procedures, several act upon nutrition indirectly, by modifying nervous reactions.

Nervous reactions, as we have already shown, play a rôle of commanding importance in pathology; their intervention is to be considered in local lesions and in general disturbances.

When a local reaction is produced, the physician may propose to exaggerate the functional derangement, to combat it, and cause its disappearance by derivation.

Medication which aims at exaggerating the functional disorder is called *naturistic*, and is frequently employed. Suppose, for instance, a case of acute peritonitis. The individual suffering from it is constipated; our treatment may consist in prescribing opium to increase the constipation, since this disorder serves to immobilize the intestine, and thus to prevent the extension of the inflammatory process. On the other hand, a purgative medicine is not infrequently prescribed for a patient attacked by diarrhœa, for the reason that the intestinal fluxion carries out microbes and toxines, and by exaggerating this fluxion we render the purification complete. For the same reason an emetic is administered in case of an attack of indigestion with nausea, and kermes, or white oxide of antimony, is given to favour expectoration. This method of therapeutics derives all its guidance from the reactions produced; it completes the work undertaken by Nature.

In certain instances therapeutics endeavours to recall disturbances which have subsided, and to awaken natural reactions which have become dormant. When a lesion has lasted for a certain length of time the process of repair may stop; the curative inflammation is not then sufficiently marked, and therefore the reaction needs to be stimulated. This is accomplished by the employment of heat, by scarifications, and by cauterizations with silver nitrate, zinc chloride, etc. In this manner the physician resumes the task undertaken and left incomplete by Nature. Tuberculin also belongs to this order of medication. This substance, as is known, represents an extract of cultures and the protoplasm of Koch's tubercle bacillus. Its introduction into a tuberculous organism gives rise to local and general

reactions which, although often very serious, may sometimes promote repair by the stimulation thus produced.

It should not, however, be assumed that naturistic indications are always to be followed; in many cases reactions are too intense, disorderly, and undisciplined, so to say, and the physician's duty is then to resort to antinaturist therapeutics. Too intense congestions and inflammations, too energetic spasmodic reactions must be combated by means of revulsives, refrigerants, and calming measures.

Finally, in case of very troublesome or dangerous manifestations, relief may be sought by means of *revulsion* or *substitution*. The old physicians often had recourse to these procedures: moxas as well as setons have rendered real service; dry or scarified cupping, sinapisms, cauterization, faradization, and hot or cold applications are still daily employed. And, though setons are out of fashion, the abscesses of fixation, such as are recommended by Dr. Fochier, amount almost to the same thing; it is a procedure rejuvenated and explained by new pathogenic views.

For disturbances resulting from congenital or acquired morbid aptitudes of the nervous system there are two orders of medications.

When reactions are too intense and irregular, sedative therapeutics should be resorted to. Materia medica furnishes some very serviceable medicines, such as the bromides, valerian, and asafœtida. The best results, however, are obtained by modifying the hygiene and mode of life of the patients. Neuropaths must lead an existence free of anxiety and dissipation. It is to be borne in mind that sorrow is in many cases the occasional cause provoking the development of a neurosis until then in a state of latency, such as hysteria, epilepsy, or mental derangements, and that the first inebriety is the starting point of dipsomania. Moreover, according to the patient's temperament— and here the physician requires perfect tact—he should be advised to travel, to live in the country or at great altitudes, or, on the contrary, to enjoy worldly distractions. Psychical treatment affords the best results in such cases. The physician must enjoy in the esteem of the patient an authority so high as to inspire him with his will, even, if needed, through suggestion. It is also to be remembered that neuropathies are hereditary. Although they may be exaggerated in the descendants to the point of appearing to be spontaneous, they already existed in the parents. In many cases the disorders are kept up by associates of the patient; under such circumstances life far from the family circle may produce marvellous results and lead to recovery. Physical procedures should be conjointly employed—e. g., progressive and rhythmical exercises, gymnastics, and, on the other

hand, massage, bathing, and douches, which are rightly too popular to need further commendation here.

When, on the other hand, the nervous system of a patient is incapable of adequately reacting, recourse is to be had to stimulations, massage, hydrotherapy, and cutaneous frictions, which act in this as in the preceding case by regulating nervous activity. At the same time various medicines should be prescribed, among which strychnine sulphate, in doses of 2 milligrammes daily, is the one most employed.

Finally, there is also a method calculated to impress the nervous system with a profound modification. This is designated as *perturbating* therapeutics, such as was commended by Trousseau. It consisted in stimulating the nervous system by large doses of active medicaments. In cases of chorea, for instance, strychnine was administered until convulsions appeared, and the nervous perturbation thus produced resulted in the disappearance of the choreic symptoms. The procedure is at present abandoned, but the method remains: the use of ice-water baths in certain grave diseases of the nerves represents a real perturbating medication.

Hygiene and Prophylaxis.—Although it is well to treat patients, it is better to give rules for avoiding disease. This last part of medicine, hygiene and prophylaxis, has to-day acquired a legitimate importance. Since the cause of infectious diseases is known and the mystery of their transmission penetrated, and since the relationship between human and animal pathology is comprehended, and precise views have been arrived at as to the necessity of disinfection and quarantine, sanitary measures have been adopted which have produced wonderful results. The extension of diseases has been prevented, epidemics have been arrested, and the number of infections reduced. The introduction of hygiene into schools, barracks, and factories has lowered morbidity and death rate in notable proportions.

Furthermore, the use of vaccination tends to cause a certain number of infectious diseases to disappear.

Vaccination.—Vaccination consists in introducing into an organism an active virus, attenuated or inoffensive, living or sterilized, in such a manner as to create a state of immunity against this virus or against another one.

The first attempts date from antiquity. The practice of variolization appears to have originated in China three thousand years ago. It spread to Persia, and then, in 1673, was introduced into Turkey by E. Timoni and J. Pylarini. In 1721, Lady Montague, who had seen its results in Constantinople, made the method known in England.

If a trace of variolous virus is inoculated into a healthy individ-

ual, a discrete, benign variola develops, conferring immunity upon him against the dangers of spontaneous smallpox. The innocuity of the inoculated variola is due to the fact that it is deposited in a tissue slightly favourable to its development, and that it is introduced into a resistant organism capable of overcoming morbid germs. The gravity of spontaneous smallpox depends, on the contrary, upon the predisposition of the subject who has permitted the development of the malady.

Nevertheless, variolization exposes to dangers. The resulting disease is quite often serious, and, at all events, it may be transmitted to those about the patient and become the starting point of an epidemic.

The method therefore is but of historical interest, at least with reference to the human species, for the active viruses of rot, of symptomatic anthrax, and of cattle pneumonia are inoculated into animals in a region in which the cellular tissue is dense and therefore not very favourable to the development of the infection—such, for example, as the tail.

There is another procedure which consists in inoculation of an inoffensive, or nearly inoffensive, virus to protect against another virus. Such is the principle of Jennerian vaccination.

It was long known in certain regions of England, and especially in the county of Gloucester, that individuals taking care of cows often presented upon their fingers small pustules contracted by contact with cattle affected with cowpox, and that such eruption rendered them immune to smallpox. In 1768, Sutton and Fewster drew attention to these facts. It was then that Jenner conceived the idea of practising in a systematic manner and with a prophylactic view the inoculation of cowpox. In 1798 he published the results of his researches; he established the inoculation of the cowpox from the cow to man, its transmission from man to man, and proved that immunization is surely conferred by inoculation of the vaccine.

The inoculation of humanized virus (Jennerian vaccine, properly so called) was preferred for a long period, but at present the animal virus is again resumed, taken directly from a vacciniferous calf or preserved in the form of glycerinized pulp.

It is hardly necessary to recall here the results obtained by means of vaccination, which, were it practised in a regular manner, would cause one of the greatest scourges of humanity to disappear forever. It is not worth while to discuss the practical side. The theory is less certain. Most authorities are of the opinion of Chauveau, that vaccinia and variola represent two distinct diseases. It has been objected to this view that we know of no infection immunizing against a differ-

ent infection. It is true that the microbe of chicken cholera and the streptococcus impart a certain degree of immunity against anthrax, but the resistance thus produced is not constant, and, at all events, is quite weak. Hence, taking ground upon clinical analogies and some experimental researches which are, however, under dispute, some authorities have asserted that vaccinia is nothing more or less than a modified smallpox. The conception is by no means illogical, since a certain number of pathogenic agents are known to be liable to such profound modifications. If the demonstration be some day rendered conclusive, Jennerian vaccination will then be considered as the first example of the inoculation of an attenuated virus, and it would enter into another method to be presently referred to.

In fact, instead of introducing active viruses, we may utilize attenuated—i. e., accidentally or experimentally modified—agents. Such is the principle of Pasteurian vaccinations.

Attenuation can be effected in a great number of procedures. Most of these consist in causing the agent to grow under dysgenetic conditions, or in disturbing its vitality by physical or chemical means. Letting the cultures grow old, submitting them to heat, exposing them to the sun, developing them at high temperatures, the addition of antiseptic substances to the medium, the influence of compressed oxygen—such are the most usual procedures. In addition to these, there are also the serial inoculations in certain animals: the virus becomes more powerful for the species experimented upon; at times it becomes weaker for another species, a result which may be regarded favourable to the original unity of smallpox and of vaccinia.

Be that as it may, the Pasteurian vaccinations are employed especially in veterinary medicine, and afford remarkable results against anthrax. Pasteur's method consists in the inoculation of two vaccines: the first, the weaker one, proceeds from a microbe which has remained in a temperature of 42° C. from fifteen to twenty days. From 1882 to 1894, 1,788,677 sheep were vaccinated in France; their death rate has been 0.94 per cent, while previously it was 10 per cent. With cattle, the death rate has fallen from 5 to 0.34 per cent.

In view of these facts, it has been a question whether vaccines would not act even after the introduction of an active virus. It was also Pasteur who took up and solved this new problem. The hydrophobic marrow, weakened by desiccation, is injected into individuals bitten by a rabid animal. In this manner it is possible to create a refractory state, which is more rapidly developed than the disease. Immunity manifests itself early enough to prevent the propagation of the active virus and to enable the organism to destroy it.

It has already several times been stated that the pathogenic agent acts only by the soluble products which it produces. This law is equally true of vaccination, as is demonstrated by numerous experiments, the first of which are due to Salmon and Smith. Sterilized cultures can therefore be substituted for the attenuated viruses; they have not, however yet been utilized in practice: there have been but a few attempts made with a view of guarding against cholera.

The preventive injection of a therapeutic serum is sometimes considered as a vaccination. In time of epidemic the antidiphtheritic serum has often been administered; the antitetanic serum is employed in wounded individuals. Thus is conferred an immunity which, unluckily, is not a lasting one. Serum therapy has not at all the same action as vaccination: it impregnates the organism with substances which are not very favourable to the development of the pathogenic agent (germicide serums), or with substances which increase the resistance of the cells against toxines (antitoxic serums). The economy becomes impregnated without reacting, and the immunity rapidly disappears as the foreign serum is eliminated: this is what is termed *passive immunity*. Vaccination, on the contrary, creates an *active immunity*; it does not introduce any germicide or antitoxic substance, but it stimulates organic reactions which result in the production of protective matters. Immunity in this case is the work of the vaccinated individual; his entire nutrition is modified for a more or less considerable period, and hence resistance is durable.

We have dwelt upon the history of vaccination because this method is one of the most admirable discoveries of modern times.

Owing to Jenner's genius, one of the most fearful diseases of the human race has almost entirely disappeared. Smallpox has become a disease of such rare occurrence that certain German authorities believe it is no longer observable in countries truly civilized; it will ere long become an infection of merely historical interest. Thanks to Pasteur's genius, anthrax diseases are disappearing in their turn; hydrophobia is becoming exceptional, and it is perhaps permissible to expect the day when tuberculosis itself will be overcome. Finally, although the mechanism is different, the serums drawn from vaccinated animals also constitute a preventive method of importance; their injection appears to be capable of preventing the development of diphtheria, tetanus, plague, and certain septicæmias, especially puerperal fever.

We can therefore perceive in the remote future the day when prophylaxis will have completely replaced medicine. It must be acknowledged, however, that for a long period of time there will yet be patients to be treated. Whenever possible, etiological medication

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must be resorted to. When the cause is inaccessible, the methods based upon pathogenesis and pathological physiology are to be employed. Finally, in a great many cases, symptomatic medication has to be made use of, no other being possible. At times even empiricism must be utilized.

Empiricism is not, as is often stated, the negation of science; it represents the first stage of science. It is an unreasoned (not unreasonable) experiment transmitted to us by tradition. It is known that such a medicament cures, although its mode of action is not understood. It is therefore right to make use of it, at the same time endeavouring to make a complete study of it. With the advance of science empirical notions will disappear, yielding their place to scientific therapeutics.

To be able to formulate rational medication many years must be spent in studying the mode of action of causes and the reactions of the organism. It is only after having made a complete theoretical study and become thoroughly familiar with modern acquisitions in etiology, pathogenesis, and physiological pathology that one can undertake medical practice. The science is the basis of the art, and therefore its teachings, even though abstract in appearance and at times of a purely speculative interest, are indispensable for the practice of medicine. Still, the study of special pathology, however important, is inadequate; before and after it, alongside of and above it, is seated general pathology, which alone can guide the physician in his career; it only can furnish the directing ideas which will conduct him to a reasoned and therefore effective therapeutics.

Table for reducing the Metric System into the English (Troy Weights)

GRAINS TO GRAMMES.	GRAINS TO GRAMMES.	GRAINS TO GRAMMES.
$\frac{1}{200} = 0.00033$	$\frac{1}{105} = 0.000628$	$\frac{1}{12} = 0.0055$
$\frac{1}{195} = 0.00034$	$\frac{1}{100} = 0.00066$	$\frac{1}{10} = 0.0066$
$\frac{1}{190} = 0.00035$	$\frac{1}{95} = 0.00694$	$\frac{1}{8} = 0.0082$
$\frac{1}{185} = 0.000357$	$\frac{1}{90} = 0.0073$	$\frac{1}{7} = 0.0094$
$\frac{1}{180} = 0.00036$	$\frac{1}{85} = 0.0077$	$\frac{1}{6} = 0.011$
$\frac{1}{175} = 0.000377$	$\frac{1}{80} = 0.0082$	$\frac{1}{5} = 0.0132$
$\frac{1}{170} = 0.000388$	$\frac{1}{75} = 0.0085$	$\frac{1}{4} = 0.0165$
$\frac{1}{165} = 0.0004$	$\frac{1}{70} = 0.0094$	$\frac{1}{3} = 0.022$
$\frac{1}{160} = 0.000413$	$\frac{1}{65} = 0.001$	$\frac{1}{2} = 0.033$
$\frac{1}{155} = 0.000425$	$\frac{1}{60} = 0.0011$	$1 = 0.066$
$\frac{1}{150} = 0.00044$	$\frac{1}{55} = 0.0012$	$2 = 0.132$
$\frac{1}{145} = 0.000455$	$\frac{1}{50} = 0.00132$	$3 = 0.198$
$\frac{1}{140} = 0.00048$	$\frac{1}{45} = 0.00146$	$4 = 0.264$
$\frac{1}{135} = 0.00049$	$\frac{1}{40} = 0.00165$	$5 = 0.33$
$\frac{1}{130} = 0.0005$	$\frac{1}{35} = 0.00188$	$6 = 0.396$
$\frac{1}{125} = 0.000528$	$\frac{1}{30} = 0.0022$	$7 = 0.462$
$\frac{1}{120} = 0.00055$	$\frac{1}{25} = 0.00264$	$8 = 0.528$
$\frac{1}{115} = 0.000574$	$\frac{1}{20} = 0.0033$	$9 = 0.594$
$\frac{1}{110} = 0.0006$	$\frac{1}{15} = 0.0044$	$10 = 0.66$

GRAINS TO MILLIGRAMMES.	GRAMMES TO GRAINS.
$1 = 64.8$	$1 = 15.43$
$2 = 120.6$	$2 = 30.86$
$3 = 194.4$	$3 = 46.29$
$4 = 259.2$	$4 = 61.72$
$5 = 324$	$5 = 77.15$
$6 = 388.8$	$6 = 92.58$
$7 = 453.6$	$7 = 108.01$
$8 = 518.4$	$8 = 123.44$
$9 = 583.2$	$9 = 138.87$
$10 = 648$	$10 = 154.3$

1 drachm or 60 = 3.89 grammes.
1 ounce or 480 = 31.1 "

Metrical Measures of Length

	In English inches.	In English feet = 32 inches.	In English yards = 3 feet.	In English miles =1760 yards.
Millimetre	0.03937	0.003281	0.0010936	0.0000006
Centimetre......	0.39371	0.032809	0.0109363	0.0000062
Metre	39.37079	3.280899	1.0936331	0.0006214
Kilometre	39370.79000	3280.892200	1093.6331000	0.6213824

1 inch = 2.539954 centimetres.
1 foot = 3.0479449 decimetres (decimetre is one tenth of a metre).
1 yard = 0.9143835 metre.
1 mile = 1.6093149 kilometre.

Formulæ for the Conversion of Degrees of Fahrenheit's Thermometer into those of Centigrade, and vice versa

F. = Fahrenheit.   C. = Centigrade.   D. = Degree observed.

If above the freezing point of water (32° F., 0° C.) :

F. into C.   (D. — 32) ÷ 9 × 5.   (For example, 104° F. = 104 — 32 ÷ 9 × 5 = 40° C.)

C. into F.   D. ÷ 5 × 9 + 32.   (For example, 37° C. = 37 ÷ 5 × 9 + 32 = 98.6° F.)

If below the freezing point of water, but above 0° F. :

F. into C.   — (32 — D.) ÷ 9 × 5.   (For example, 14° F. = (32 — 14) ÷ 9 × 5 = — 10° C.)

C. into F.   32 — (D. ÷ 5 × 9).   (For example, — 16° C. = 16 ÷ 5 × 9 = 28.8 and 32 — 28.8 = 3.2° C.)

If below 0° F. :

F. into C.   — (D. + 32) ÷ 9 × 5.   (For example, — 22° F. = 22 + 32 ÷ 9 × 5 = — 30° C.)

C. into F.   — (D. ÷ 5 × 9) — 32.   (For example, — 20° C. = 20 ÷ 5 × 9 — 32 = — 4° F.)

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THE END

THE PRINCIPLES AND PRACTICE OF MEDICINE.

By WILLIAM OSLER, M. D.,

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